AN INTRODUCTION TO GASTRO ENTEROLOGY

"*I am convinced that it is by frequent interchange* of opinion between the physiologist and the phy sician that the common goal of physiological science and of medical art will be most quickly and safely reached

—Ivan P Pavlov

# AN INTRODUCTION TO GASTRO-ENTEROLOGY

FOURTH EDITION, REVISED AND ENLARGED

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WITH 269 ILLUSTRATIONS



PAUL B HOEBER INC
MEDICAL BOOK DEPARTMENT OF HARPER & BROTHERS
NEW YORK

AN INTRODUCTION TO GASTRO ENTEROLOGY

BEING THE FOURTH EDITION OF

THE MECHANICS OF THE DIGESTIVE TRACT



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PUBLISHED
NOVEMBER 1948

# PREFACE TO THE FOURTH EDITION

TO BRING THIS BOOK UP TO DATE I HAVE GONE through the physiologic and the bordering literatures since publication of the third edition and have inserted here abstracts of well over 400 articles and books which I thought were important The bibliography now runs around 2800 titles

The heaviest additions have been made to the chapters on the pylorus the nerves running to the bowel the nerves of the gall-bladder, the functions of the colon flatulence the electro entero gram, and technical methods and apparatus

Because of the present day interest in the Dragstedt operation I have added much information as to the effects of vagotomy in man

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# PREFACE TO THE THIRD EDITION

THIS IS PRACTICALLY A NEW BOOK ENTIRELY RE written, about doubled in size reinforced by the experience gained in laboratory and clinic in the last eleven years and made richer by data taken from some 1500 new articles and books In all seven new chapters have been added

I first wrote and later rewrote this book to make readily available to students teachers, physicians, and research workers much information which otherwise they might never run onto I want to help young men to get oriented quickly, so that those with a gift for research can start off intelligently and on good problems in their youth when they are full of enthusiasm and new ideas and most

likely to do big things It is unfortunate that many would-be research workers choose poor problems and poor methods Often they do not know that the particular question they propose to answer is of little interest, or worse yet, that it has been answered already many times What they need to know is where the big gaps in our knowledge are—gaps that should be filled, and when they start work they should know what precautions must be taken if the results of their experiments are to be decisive, and their conclusions unquestioned

As the literature of science becomes ever larger, it becomes more and more necessary that we older men make efforts to help the younger ones with their reading We must try to lift them up and start them off from the level of our intellectual shoulders Obviously, they cannot begin by reading all we have read in forty years! That small part which we have found useful should be taken out and summarized for them and then we must show them where to look in the library for the most important papers and books and review articles

The student looking for a problem for research will sometimes get the idea that all likely ones have already been tackled, but he need only open this book at almost any page to find a problem crying out for a definite answer

I have taken particular pleasure in preparing Chapter XXXIV on the source books and articles to which the student can turn for a quick entree into the several phases of the literature of gastro enterology and gastro-intestinal physiology Chapter XXXIII on technical methods will, I think be found useful by laboratory workers

With the idea of saving the time of the student and the tired and hurried practitioner who wants but a brief answer to some question I have added a summary to each chapter

I would like to correct here an impression which many men seem to have carried away from a cursory reading of the previous editions of this book, and this is that my principal theme is that all the motor activities of the digestive tract are purely muscular in origin Actually, as the student can see from a glance at the summaries to Chapters II and X what I say is that many men have found that the digestive tract *can* in some individual animals get along and do its work after degenerative section of the extrinsic nerves but it is then likely

to be handicapped by excessive irritability I say also that almost every bit of evidence including that of Magnus, indicates that the *local rhythmic movements* of the small intestine *could* go on if all nerve tissue *could* be removed, but as this has not yet been done and probably can never be done to everyone s satisfaction the question must remain open In the rabbit, but perhaps not in the dog, the extrinsic nerves of the bowel appear to keep the rate of rhythmic contraction faster than it would otherwise be

I have been careful never to say that the *peristaltic rushes* are independent of nerves because the available evidence indicates that ordinarily they run down the bowel with the help of a local synaptic nervous system

Actually in emphasizing the *facultative* autonomy of the digestive tract and the smooth muscle in it I had no desire to start a useless controversy All I wanted to do was to correct false statements in the literature and to show students that almost all the functions of the bowel can be looked for and studied locally and not in far off ganglions Just one glance at a rabbit s bowel functioning beautifully when excised and thrown into a tank of warm aerated Locke s solution should be enough to convince anyone on this point

I regret that in the past I have not thought clearly enough about the gradient idea to distinguish always between the polarization of the bowel and the gradients In this edition I have shown that the small bowel is undoubtedly polarized in that every short segment conducts better in one direction than another this is a fact that has been observed by several physiologists Gradients of several kinds can be found along the length of the bowel and this also is a fact that has been observed by several physiologists What now remains to be learned is What relation have the gradients to the polarization? I think it probable that the two facts of observation are related, but some puzzling questions still remain to be answered I feel sure that the best and simplest explanation available for the usual aboral progress of food down the bowel is the polarization of the muscular wall and I believe one of the best ways of attacking the problems of polarization is to study the gradients

Incidentally no one should attempt to explain the progress of material through the bowel until he has studied in several species of

have been confirmed The whole *gradient idea has been strengthened* by the work of *Murray, who has shown that even in tissue cultures,* muscle cells from the embryonic auricle *will beat many times faster* than will those from the ventricle This must mean, as Dr Child and I have always felt, that the gradients are not due purely to functional adaptation during life but that they are basic, and built into the very structure and chemical composition of the individual cells

The bibliography of the present volume containing 900 titles is probably the best part of the book The papers referred to have all been read or looked over by me, and their messages incorporated in the text I know that I must have missed or forgotten many good articles, but the literature is now so enormous that even a fast reader can hardly keep up with it and from those whose good work I have slighted I can only beg forgiveness, and a reprint

Some may perhaps doubt the propriety of publishing as I have done here the likenesses of living contributors to the subject under discussion, but I could see no *valid reason* why the *readers* of this book *should not share the pleasure and inspiration that is mine each day as I glance at the gallery that adorns the walls of my laboratory* It does us good to know those who have taught us much, and we are the better for having literally and figuratively looked up to them

It is a pleasure to acknowledge here my indebtedness to my wife for her help with the proof sheets, and to my colleagues Drs Balfour, Eusterman, Mann, McVicar, and Vinson, who were kind enough to read some of the chapters in manuscript and to make helpful suggestions and criticisms, and to my friend Paul Hoeber for his faith in me and my work I feel also that I cannot close this book without making some acknowledgment of the great debt I owe to the men who have so generously dedicated to research medicine all the profits of a great institution, and have thereby *set free from routine tasks a group of men who like myself love to study and experiment* If I *had gone on carrying the burden of private practice* it is doubtful if I would ever have had the courage to start on this edition, or the time and strength to finish it

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# GASTRO ENTEROLOGY



# CHAPTER I

# THE MOTOR FUNCTIONS OF THE SMALL BOWEL

THE GASTRO ENTEROLOGIST SHOULD ALWAYS KEEP in mind two facts one that the important organ of digestion is the small bowel and the other, that most of the symptoms of indigestion appear to arise in disturbances in the *motor functions* of the digestive tract

Before trying to see *why* the bowel works as it does, it would be well to see *how* it works In this chapter I shall first mention briefly the several types of activity in the small bowel, and then I shall describe them in more detail

### TWO MAIN TYPES OF ACTIVITY

As everyone knows there are two main types of activity in the small bowel one, a more or less local one designed mainly to knead the intestinal contents and to rub them over the absorbing surface and the other a traveling contraction designed to move material from one segment to the other

These activities are somewhat different in different animals and in different parts of the small bowel in any one animal Thus, I do not remember ever having seen in the dog the type of rush wave that is common in the rabbit, and I have seldom seen in the rabbit the type of rhythmic segmentation that is so typical in the cat Furthermore *rhythmic segmentation is far more likely to appear in the* jejunum than in the ileum

The to and fro swaying movements so typical of the small bowel of the rabbit serve the same purpose as do the rhythmic segmentations in other animals The difference may be that the successive centers for contraction are farther apart in the rabbit than in the cat and a greater length of bowel contracts as a unit

It is not generally recognized that the rhythmic segmenting movements assist in the forwarding of the intestinal contents This can be shown best by taking roentgenocinematographic pictures of rhythmic segmentation, transferring these pictures to 35 or 16 mm film, and running the film through a projector at two or three times the speed at which the pictures were taken One then finds that the segmentations which had appeared to take place, now above and now below one spot, were really advancing caudad along the bowel and at frequent intervals biting off a little bolus of food and forcing it into the quiet gut immediately distal to the active region

Zimmermann and I first noted this progression of the rhythmic swaying movements of the small bowel of the rabbit when, by plotting on paper (as ordinates) the changing distances between adjacent marks made on the gut, as recorded in the successive frames of a motion picture film, we obtained a series of sine-like curves When these were placed in a series, one below the other corresponding to the position of the respective markers on the gut, and all on the same abscissal scale, the peaks and troughs fell along lines slanting downward to the right This indicated that waves were traveling down the bowel Actually they didn't go far before the sequence was broken by a sort of interpolated extrasystole If the waves starting in the duodenum were to continue on to the ileum uninterrupted the rate of rhythmic activity would have to be the same in the ileum as in the duodenum, when actually, as I shall show later this is not the case The rate is graded from approximately twenty-two contractions a minute in the duodenum to approximately twelve a minute in the terminal ileum Similar analyses of motion pictures of segmenting bowel in cats made by Hukuhara and Roden showed the same tendency to progression which I observed Roden's records indicated also that each time the bowel contracted for a rhythmic segmentation it gave the contents a quick push caudad and then a slower one orad

In addition to the big rush waves there appear to be other, more slowly traveling contractions which, particularly in the dog cause boluses or balloons to traverse segments of small bowel isolated as Thiry-Vella fistulas Because with the usual technic these waves cannot be seen, little is known about them They can best be studied in segments of exteriorized bowel, and with this technic Castleton

saw, particularly in the jejunum (of the dog), a series of little waves traveling caudad

There are also tonus waves which are to be found in many of the records made of intestinal activity Usually these waves have superimposed upon them the more rapid rhythmic contractions but occasionally they *appear on the records as simple sine curves In cases of* experimentally produced intestinal obstruction in the rabbit, I gained the impression that these tonus contractions were moving slowly caudad They *then resembled the waves of the stomach and colon*

There is another type of contraction to be observed in the small bowel and this is what I call a systole because long stretches of bowel contract at the same moment One sees also reverse waves waves that run both ways from a given point, and waves that run orad over bowel which at the time is transmitting waves caudad

Finally, it should be remembered that fluids commonly spread out and trickle through long segments even of boiled bowel much as they would spread out through a piece of hose lying on the ground Some of this transport of fluid may be due to large tonus changes in long segments of bowel contractions which cause a narrowing of the lumen together with much shortening of the affected segment

There seems also to be a transport of material along the surface of the mucosa Years ago Grützner (1894, 1898) claimed to have demonstrated the progress of bacteria or small particles of carmine against the current from rectum to stomach and for a while there was much discussion of the subject some observers confirming and others denying the existence of the phenomenon (see Chapter VIII)

There are probably other types of intestinal activity in other ani*mals such as the guinea pig and white rat types which need to be* correlated with the somewhat different activities seen in the much studied rabbit

*Peristalsis is a carelessly used term* If confusion is to be avoided it is essential that everyone who writes about the movements of the bowel use certain terms carefully and exactly At present the term peristalsis is being used carelessly to mean any or all forms of motor activity in a segment of bowel To begin with this is flouting the dictionary The American Medical Dictionary defines peristalsis I believe correctly as a worm like movement by which the alimen

CHAPTER VI —*continued*



## CHAPTER VII

CHAPTER VIII —*continued*

CHAPTER VIII—*continued*



## CHAPTER IX

## CHAPTER X

CHAPTER X—*continued*



## CHAPTER XI

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## CHAPTER XIII



## CHAPTER XIV

## CHAPTER XV



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## CHAPTER XVII



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## CHAPTER XX



## CHAPTER XXI



## CHAPTER XXII



## CHAPTER XXIII

# INTRODUCTION

HEART disease is by far the most common cause of natural death in civilised communities in the more temperate zones of the world It is responsible for at least two fifths of all such deaths and for an annual mortality rate in the general population of about 0 45 per cent Both incidence and mortality curves have been rising steadily for many years a fact which is not fully explained by ageing populations and by the control of infectious fevers pulmonary tuberculosis and pyogenic infections The incidence and mortality of cancer for example show no comparable increase Ischæmic heart disease particularly is becoming more frequent

It is by no means easy to estimate the prevalence of each kind of heart disease for selection plays havoc with most personal and hospital statistics whilst random samples usually suffer from inaccurate diagnosis For example amongst a consecutive series of 10 000 cases of cardiovascular disease that I have seen personally during the last few years 900 or 9 per cent had congenital heart disease which is about six times the number that would be expected in a random sample of cardiovascular cases The other side of the picture is illustrated by the Registrar General s statistical review for 1953 in which the chief cause of all deaths is myocardial degeneration a diagnosis which is not recognised in cardiovascular clinics whilst cor pulmonale is not mentioned at all Nevertheless an attempt has been made to assess the prevalence of the more important forms of heart disease based on the literature my own data and the Registrar General s statistical reviews A few general observations may be made first

The population of England and Wales in 1953 was approximately 44 000 000 There were 503 529 deaths during this year Of these 183 917 were due to heart disease 68 069 to a cerebral vascular accident and 30 392 to bronchitis and emphysema At least half of all the deaths were therefore cardiovascular and over half if cor pulmonale had been included For comparison there were 89 680 deaths from neoplasm (of which 15 132 were due to carcinoma of the lung) 20 759 from pneumonia and 8 902 from tuberculosis

The ensuing table is no more than an approximate estimate of the incidence of the more important kinds of heart disease and the many blanks represent lack of reliable information

## INCIDENCE OF CHIEF FORMS OF HEART DISEASE

| | PERCENTAGE OF CLINICAL CASES OF HEART DISEASE | PERCENTAGE OF POPULATION | PERCENTAGE OF CARDIAC DEATH | PERCENTAGE OF ALL DEATHS |
|---|---|---|---|---|
| Bacterial endocarditis | 1 0 | — | 0 17 | 0 07 |
| Congenital heart disease (*surviving infancy*) | 1 5 | 0 1 | 0 9 | 0 36 |
| Cor pulmonale | 5 0 | — | 5–15 | 2–6 |
| Dissecting aneurysm | 0 [illegible] | — | 0 45 | 0 18 |
| Hyperkinetic circulatory states | 0 3 | — | — | — |
| Hypertension | 25 0 | 3 0 | 10 0 | 4 0 |
| — cerebral vascular accidents | — | — | — | 13 5 |
| Ischæmic heart disease | 30 0 | [illegible] 0 | 31 [illegible] | 12 5 |
| Miscellaneous and uncertain | 6 5 | — | — | — |
| — degenerative | — | — | 35 0 | 14 0 |
| Myocarditis and other rare or obscure cardiopathies | 0 3 | — | — | — |
| Pericarditis (primary) | 1 0 | — | — | — |
| Pulmonary embolism | — | — | 6 5 | 2 6 |
| Pulmonary hypertension (primary or thrombo embolic) | 0 [illegible] | — | — | — |
| Rheumatic carditis | 5 0 | 0 5 | 0 15 | 0 06 |
| Rheumatic heart disease (chronic) | 15 0 | 1 5 | 4 5 | 1 8 |
| Rhythm changes—primary | 5 0 | — | — | — |
| Syphilitic aortitis | 1 0 | — | 0 5 | 0 2 |
| Thyrotoxic heart disease | [illegible] 0 | — | 0 [illegible] | 0 08 |

CHAPTER I

# THE CHIEF SYMPTOMS OF HEART DISEASE

## HISTORY TAKING

TO take an accurate and relevant history is one of the most difficult and important arts in medicine Sometimes a complete diagnosis can be made from the history alone and not infrequently the possibilities can be whittled down to two or three A good history should at least indicate the system involved or it should point unerringly to some group or groups of diseases A common mistake is the failure to analyse any given symptom sufficiently in cardiovascular work this applies especially to pain breathlessness palpitations and syncope The student is usually taught to encourage the patient to tell his story in his own words and to record them more or less verbatim Yet such an account may be verbose irrelevant inaccurate and misleading It is an axiom that the leading question must be avoided at all cost yet again an experienced physician must know that the ability to put the appropriate leading question at the right moment and the intelligent interpretation of its reply are invaluable It is not pretended that leading questions may not lead to false information if the power of their suggestion is not appreciated by the questioner and it is agreed that much may be lost by failure to allow the patient freedom and time to express his complaints in his own way but the average patient will not mention half the available information until he is pressed and the data freely given must be checked as at the bar For example in the differential diagnosis between a neural and non neural somatic lesion an accurate description of the quality of the pain may determine the issue immediately yet the majority of patients will volunteer no information concerning the quality of pain and if asked to describe it will do so inadequately They may say it is aching or sharp but fail to enlarge on this even when urged to do so In answer to the leading question Does it tingle? however they may reply at once in the affirmative It is essential to realise that the matter does not end there that such a positive reply to a leading question demands the most penetrating cross examination until the questioner is satisfied that the pain really does tingle and that the patient is not merely saying so because it seems the easier answer It is scarcely too much to say that the best history taker is he who can best interpret the answer to a leading question Appropriate leading questions can only be asked however when the proffered history has provided sufficient data upon which to work and if the physician has sufficient knowledge of the possibilities then entailed It is this latter factor which makes it easier for the expert than for the student

## SYMPTOMS

The symptoms of heart disease vary considerably according to the nature of the cardiopathy and the kind of physiological disturbance in the circulation that results each will be discussed in particular relation to the form of heart disease in which it occurs in subsequent chapters, but it may help here to survey the subject in general

To begin with it should be thoroughly understood that cardiovascular disease may be severe without any symptoms whatever good examples of this axiom are coarctation of the aorta pulmonary stenosis atrial septal defect *aortic stenosis malignant hypertension primary pulmonary hypertension* and aortic aneurysm even cardiac infarction may be silent

A second point of general interest is that patients rarely appreciate what is a heart symptom and what is not The most classical example of this is the well known paradox that patients with angina pectoris (including doctors) often complain of indigestion whereas those with dyspepsia or left inframammary pain may be convinced that their hearts are at fault Headaches and dizziness are frequently attributed to high blood pressure when there is no hypertension palpitations which are usually innocent, are a common source of anxiety fatigue and lack of energy resulting from psychological conflict are often ascribed to failing circulation On the other hand breathlessness due to mitral stenosis or left ventricular failure may be attributed to bronchitis, an attack of paroxysmal cardiac dyspnœa to bronchial asthma and coughing from pulmonary venous congestion to over smoking A man with gross congestive heart failure has even been known to present himself first at a skin clinic on account of pruritis (due to jaundice)

Finally after recording the symptoms faithfully in chronological order the absence of any important symptom that might reasonably have been expected under the clinical circumstances should also be noted In a case presenting with mitral stenosis for example with effort breathlessness of moderate grade as the only positive symptom, an experienced physician would record the absence of hæmoptysis winter bronchitis orthopnœa *paroxysmal cardiac dyspnœa angina pectoris, recurrent palpitations* peripheral embolism and œdema because all these are important symptoms of mitral stenosis each having its own particular meaning On the other hand he would not record the absence of syncope squatting transient cyanosis headache heat intolerance Raynaud s phenomenon and a host of other negatives which under the clinical circumstances are irrelevant The recording of a negative implies that the appropriate leading question has been asked

### *PAIN*

*Cardiac pain* is ischæmic being due to stimulation of afferent nerve endings in the myocardium by metabolites resulting from oxygen deficiency in working muscle

The commonest cause is occlusive coronary atherosclerosis In *simple angina pectoris* the coronary flow is adequate at rest but becomes inadequate when the demands of the myocardium are increased by exercise In *acute coronary insufficiency* the flow suddenly becomes inadequate at rest usually as a result of thrombosis but is still sufficient to prevent necrosis In *acute cardiac infarction* failure of the coronary flow to part of the heart muscle leads to ischæmic necrosis (gangrene)

Pain in angina pectoris is characteristically central in position pressing in quality brief in duration and closely related to effort It is felt more across the chest than in the mid line and may radiate to the shoulders down both arms into the neck or jaws and through to the back It is usually described as heavy or squeezing but may be bursting burning or like indigestion It occurs especially on walking particularly after meals on a cold day against the wind or uphill It forces the patient to stop or slow down and disappears in two or three minutes when he stands still In acute coronary insufficiency the pain also occurs at rest lasts longer and is often more severe and in cardiac infarction it continues for hours, even for a day or two

The chief cause of a sudden increase in the frequency or duration of cardiac pain is coronary thrombosis whether it leads to cardiac infarction or not Coronary occlusion due to subintimal hæmorrhage is rare Diabetes mellitus myxœdema, xanthomatosis and familial or idiopathic hyper cholesterolæmia are often complicated by angina because they encourage atherogenesis Thromboangiitis obliternans polycythæmia vera, shock and trauma may be complicated by cardiac infarction because they encourage coronary thrombosis Infarction secondary to subintimal hæmorrhage may be caused by injury to the chest or too vigorous anticoagulant therapy

Angina may also be caused by any condition which adversely disturbs the balance between cardiac work and coronary blood flow There are four classical examples (1) severe hypertension may cause angina when the coronary arteries are normal because the work of the heart is increased by the high peripheral resistance (2) any of the hyperkinetic circulatory states such as thyrotoxicosis may encourage angina by increasing cardiac work in respect of the volume pumped (3) angina in syphilitic aortitis is due to reduction of coronary flow owing to obstruction at the mouths of the coronary arteries, (4) angina during a paroxysmal rhythm change with rapid ventricular rate is due to the poor coronary flow that results from the shortened periods of diastole

In the presence of healthy coronary arteries physiological work and normal coronary flow angina may yet occur if the oxygen supply is deficient This is the chief cause of cardiac pain in severe anæmia although extra work due to a raised cardiac output is contributory Angina similarly provoked might be expected in anoxic cor pulmonale but it is uncommon and when present may well be due to coincidental coronary disease Angina rarely occurs from anoxia in cyanotic congenital heart disease Finally

mechanical obstruction to the circulation may cause angina by strictly limiting the cardiac output and hence the coronary flow while increasing the work of the heart Examples include aortic stenosis mitral valve disease, pulmonary hypertension massive pulmonary embolism and pulmonary stenosis

*Pericardial pain* is usually sharper more left sided than central and may be referred to the neck or flank It is relatively long lasting and independent of effort

Pain from *aneurysm of the aorta* is usually due to pressure erosion and from *dissecting aneurysm* to a variety of causes including stripping of the adventitia involvement of the segmental arteries coronary occlusion and hæmopericardium

Despite the characteristic nature and behaviour of cardiac pain the vast majority of lay persons believe it is situated in the region of the left breast *Innocent left inframammary pain* is therefore one of the commonest symptoms that brings a patient to seek medical advice This pain is a long lasting dull ache momentarily accentuated from time to time by sudden sharp jabs it is situated well to the left bears no direct relationship to effort may prevent the patient lying on the left side and is often associated with superficial tenderness Thus it differs radically from angina pectoris in site quality duration and behaviour, i e in all four major characteristics

*Other varieties of chest pain which may have to be distinguished from* angina pectoris include pain referred from the spine œsophagus stomach duodenum gall bladder and mediastinum and local pain arising from structures in the chest wall such as muscles and ligaments

## *DYSPNŒA*

Breathlessness is the most common and perhaps the most important of all symptoms relating to heart disease and also the most complex The physiology of cardiac dyspnœa is discussed more fully in the chapters on special techniques (respiratory function) heart failure and mitral stenosis

Shortness of breath like all other symptoms is subjective and the intensity of the sensation depends in no small measure on the patient s acuteness of perception Individual variation is great and explains why under exactly similar physiological circumstances one patient appears to be incapacitated while another carries on his normal occupation with relative tranquillity

*Hysterical dyspnœa or hyperventilation* is rather different for here the added stimulus to breathe is purely cortical and the activity may continue in the presence of true alkalæmia and oxygen supersaturation A similar situation may occur in encephalitis Hyperventilation may also be caused by various proprioceptive impulses such as pain and especially from activity of voluntary muscle as on exercise (Comroe and Schmidt 1943)

The simplest form of dyspnœa is suffocation The intense desire for breath is due to direct stimulation of the respiratory centre by a *rising*

*carbon dioxide tension* (Haldane and Priestley 1905) and reflex stimulation from *arterial hypoxia* acting on chemoreceptors in the carotid and aortic bodies (Heymans *et al*, 1939) Breathlessness of this kind occurs in asphyxia from any cause e g drowning strangulation peripheral respiratory paralysis tracheal obstruction, severe bronchial asthma advanced emphysema bilateral pneumothorax and acute pulmonary œdema *The fault lies with ventilation* an insufficient number of alveolæ are filled with fresh air at each breath

A second easily understood form of dyspnœa results from *breathing ill conditioned air* i e air with too low an oxygen content or too high a carbon dioxide content Ventilation is normal but the gases are at fault

A third form is encountered in diabetic acidosis and uræmia Here both ventilation and inhaled gases are normal but *the arterial pH is low* and it is this which excites the chemoreceptors

Hypoxia may result from *structural change in the alveolar walls* so that proper interchange of oxygen between alveolar air and pulmonary capillary blood is hindered This may occur when there is widespread interstitial fibrosis of the lung

Hypoxic dyspnœa associated with hyperventilation also occurs in cases of *right to left intracardiac shunt* as in Fallot s tetralogy

A sixth major cause of dyspnœa is severe anæmia when there is *insufficient hæmoglobin* to carry the oxygen

Rapid shallow breathing may result from *hyperactivity of the reflex described by Hering and Breuer* (1868) whereby relatively little inflation of the lungs arrests inspiration this is the type of dyspnœa seen in pneumonia

None of the above mentioned mechanisms accounts for ordinary cardiac dyspnœa In left ventricular failure and mitral stenosis dyspnœa is closely related to pulmonary venous congestion both arterial oxygen and carbon dioxide content are normal and the cardiac output at rest is not necessarily reduced The difficulty in breathing is attributed to *greater resistance on the part of the turgid lungs to both inflation and deflation* so that the muscles of respiration have to work harder a higher negative intrathoracic pressure is required for inspiration and even a slight positive pressure may be necessary for expiration (Christie and Meakins 1934)

In heart failure without pulmonary venous congestion from primary pulmonary hypertension or pulmonary stenosis for example dyspnœa is far less pronounced but it is still present and requires a different explanation The cardiac output is lower in these cases and the arterio venous oxygen difference higher so that increased ventilation may be necessary to ensure full oxygenation of the grossly unsaturated blood arriving in the lungs This hyperventilation may be chemically induced by *tissue hypoxia resulting from the low cardiac output* (Gesell 1925)

Special varieties of dyspnœa known as orthopnœa paroxysmal cardiac dyspnœa cardiac asthma and Cheyne Stokes breathing are fully discussed in the section on heart failure (Chapter VII)

## ŒDEMA

When due to heart disease œdema is a sign of failure It is attributed to sodium retention as explained in Chapter VI and in a sense therefore is renal in origin In the majority of cases it is associated with a low cardiac output and a raised venous pressure The latter is due partly to elevation of the right ventricular end diastolic pressure and partly to the hydræmia resulting from sodium retention it is not itself responsible for the dropsy

There are many causes of œdema other than heart failure and although most of them are well known serious errors in etiological diagnosis are still all too common A brief review of the subject will not therefore be out of place here

Physiologically it is thought that water, electrolytes and certain other small molecules such as sugar and urea, leave the blood stream at the arterial end of the capillaries and re enter at the venous end the forces at work including the hydrostatic and osmotic pressures within and without the vessels and the permeability of the vascular endothelium At the arterial end of the capillary the hydrostatic pressure exceeds the osmotic at the venous end it is the other way about Thus the hydrostatic pressure on the arterial side of a capillary loop averages about 31 mm Hg and on the venous side about 12 mm Hg (Landis 1929) the tissue pressure outside the wall of the capillary is only 2 or 3 mm Hg (Burch and Sodeman 1937) and the effective colloid osmotic pressure of the plasma is usually said to be about 25 mm Hg It has been calculated by Krogh (1929) that the total capillary filtering surface in man is about 6 300 square metres The normal state of fluid balance may be upset in favour of the tissues by raising the hydrostatic pressure within the capillaries or reducing it without by reducing the osmotic pressure within the capillaries or raising it without or by increasing the permeability of the vascular endothelium (Starling 1895–6)

Increased hydrostatic pressure at the venous end of the capillaries is the cause of *œdema in venous thrombosis* cirrhosis of the liver with tense ascites and in partial or complete *obstruction of the superior or inferior vena cava* Low extra capillary pressure may determine the site of œdema but does not cause it Lax tissue occurs naturally in certain situations e g in the infraorbital region and may be demonstrated subcutaneously following considerable loss of weight or when the skin has been stretched by previous dropsy Reduction of capillary osmotic pressure is due mainly to reduction of plasma albumin Œdema usually develops when the total blood proteins fall below 5 G per cent *Nephrosis protein starvation severe chronic anæmia* and *gross protein loss* in pleural or peritoneal exudates may provide examples of such œdema The chief effect of increasing the permeability of the capillaries is to allow more albumin to escape into the tissue spaces (a certain amount escapes normally and re enters the blood stream via the lymphatics) and so to increase the osmotic pressure of the tissue fluid

Œdema with a high protein content (3 to 4 G per cent) results Such œdema may be associated with *burns*, *trench feet insect bites* and *allergy* (e g Quincke s disease) *Lymphatic œdema* has a similar high protein content but is also rich in cholesterol (White and Sachs 1950)

Œdema due to *sodium and water retention* is associated with hydræmia This raises the hydrostatic filtering pressure of the capillaries and lowers the osmotic pressure Physiologically, the amount of water retained or excreted is controlled by the hypothalmus via the neurohypophysis osmo receptors in the hypothalmus react to dilution of the plasma by inhibiting the liberation of anti diuretic hormone by the neurohypophysis so that diuresis results on the other hand if the plasma becomes more concentrated an increased quantity of anti diuretic hormone is liberated and the flow of urine is suppressed (Verney 1946) Physiological hydræmia sometimes accompanied by slight œdema occurs during the *premenstrual phase* in women (Frank 1931) and has been attributed to elevation of the œstradiol progesterone ratio (Greene and Dalton 1953) This also may act by stimulating the liberation of anti diuretic hormone

*Famine œdema* is complex It may be associated with thiamine deficiency (wet beri beri) or with serious reduction of plasma proteins (Denz 1947) but in other cases neither of these factors can be held responsible this last group is characterised by diuresis in the horizontal position and with enlargement of the adrenal glands (Sinclair 1948)

*Renal œdema* is discussed in Chapter XI

In practice the causes of œdema most often confused with cardiac œdema are Milroy s lymphatic deficiency, premenstrual hydræmia bilateral phlebo thrombosis and chronic nephritis

## *FATIGUE*

Since fatigue cannot be seen like laboured breathing or œdema it is apt to be underestimated as a symptom of heart failure yet it is as closely related to a low cardiac output as dyspnœa is to pulmonary venous con gestion Thus patients with tight mitral stenosis and a low pulmonary vascular resistance complain of dyspnœa for the chief physiological result of the situation is pulmonary venous congestion but if the pulmonary vascular resistance is extreme congestion of the lungs is relieved at the expense of right ventricular failure and a low cardiac output, and dyspnœa is replaced by fatigue

Patients complain of heaviness of the limbs on exertion weakness or lack of vigour or general tiredness and exhaustion The physiology of such fatigue is too complex and ill understood to discuss here with profit The practical problem is to distinguish cardiac fatigue from that due to anxiety or other mental conflict This is rarely difficult for cardiac fatigue is related to effort and is always associated with genuine signs of congestive heart failure

## CYANOSIS

Cyanosis is a physical sign rather than a symptom but since it often looms large in a patient s history it may be best considered here

It is well known that a blue colour is imparted to the skin when the capillary blood contains 5 G or more of reduced hæmoglobin per cent (Lundsgaard 1919) Thus with a normal quota of hæmoglobin (15 G per cent) at least one-third of it must be in the reduced form in the capillaries for cyanosis to appear Normal arterial blood is 95 per cent saturated with oxygen i e 14 25 of the 15 G per cent of hæmoglobin in the arterial blood is oxyhæmoglobin and only 0 75 G reduced hæmoglobin The normal mixed venous blood is about 70 per cent saturated with oxygen i e 10 5 G per cent of the hæmoglobin in venous blood is oxyhæmoglobin and 4 5 G reduced hæmoglobin The amount of reduced hæmoglobin in capillary blood is assumed to be the mean between arterial and venous contents thus in a normal individual at rest capillary blood would be assumed to contain $\frac{0\ 75\ G + 4\ 5\ G}{2}$ of reduced hæmoglobin per cent, or 2 6 G per cent The colour of the normal skin and mucous membranes is therefore pink not blue

A corollary of Lundsgaard s thesis is that cyanosis cannot appear in anæmic subjects if the hæmoglobin is less than 33 per cent for even if all the hæmoglobin was then in the reduced form in the capillaries the total amount would still be less than the critical level of 5 G per cent In polycythæmia on the other hand a total of 5 G per cent of reduced hæmoglobin in the capillaries is readily achieved

While the colour of the skin and mucous membranes depends on the amount of reduced hæmoglobin in the capillaries the intensity of the hue is determined by the physical state of the capillaries if they are dilated the colour is rich if they are constricted the colour is pale

*Cyanosis may be central or peripheral Central cyanosis* means that the arterial oxygen saturation is low It can usually be detected clinically when the arterial oxygen saturation falls below 85 per cent With a normal hæmoglobin arterial blood contains 3 G per cent of reduced hæmoglobin when 80 per cent saturated with oxygen If the cardiac output is normal the mixed venous blood is then about 60 per cent saturated and contains 6 G of reduced hæmoglobin per cent The capillary mean thus works out at $\frac{3+6}{2}$ G per cent or 4 5 G per cent

With 85 per cent arterial oxygen saturation a normal cardiac output and 100 per cent hæmoglobin, mean capillary blood contains about $\frac{2\ 25+5\ 25}{2}$ or 3 75 G of reduced hæmoglobin per cent Yet in Fallot s tetralogy under just these conditions cyanosis can be detected clinically

In a group of fifteen acyanotic cases of Fallot s tetralogy studied by

the author the arterial oxygen saturation ranged between 87 and 97 per cent at rest anything less than this gave rise to clinical cyanosis except in one case with anæmia

Cyanosis in cor pulmonale due to emphysema may also be clinically detected when the arterial oxygen saturation falls below 85 per cent even when the cardiac output is raised and the arterio venous oxygen difference reduced In six such cases studied by the writer and in which the arterial oxygen saturation ranged between 78 and 87 per cent the mean capillary blood contained an average of 3 9 G of reduced hæmoglobin per cent

These observations do not tally with Lundsgaard s figure of 5 G per cent quoted earlier but the calculations are based on mixed venous samples obtained from the right atrium not from blood obtained directly from the skin veins We have no data on how such samples would effect the calculations It is observed however, that ordinary venous blood containing 4 5 G per cent of reduced hæmoglobin is obviously blue

Central cyanosis occurs in congenital heart disease with right to left shunt as in Fallot s tetralogy in arterio venous fistula of the lung and in certain pulmonary diseases such as severe emphysema which interfere with alveolar function, so that blood passing through the lung is incompletely oxygenated Central cyanosis is usually associated with polycythæmia although this may be masked by a high blood volume as in many case of cor pulmonale If sufficiently severe and long lasting it is also associated with clubbing of the fingers and toes

*Peripheral cyanosis* may be a manifestation of a low cardiac output the tissues extracting more oxygen from each 100 ml of blood because of the limited supply *but heart failure must be extreme before the mean capillary* blood contains sufficient reduced hæmoglobin to cause cyanosis in warm territories such as the conjunctivæ Thus of 20 cases with an extreme pulmonary vascular resistance (averaging 15 units or 1 200 dynes sec /cm 5) due to primary pulmonary hypertension (6 cases) or secondary to mitral stenosis (14 cases) chosen at random provided the cardiac output was below 4 litres per minute (in fact it averaged 3 l /min ) the mean capillary blood contained an average of 4 17 G of reduced hæmoglobin *per cent* None of these cases had cyanosis of the conjunctivæ or other mucous membranes yet the amount of reduced hæmoglobin in the capillaries calculated in the customary fashion was often as high or even higher than that found in cases of Fallot s tetralogy with arterial oxygen saturations around 80 per cent and obvious though mild central cyanosis Mixed venous samples had a higher content and arterial samples a lower content of reduced hæmoglobin in these low output cases than in the examples of Fallot s tetralogy mentioned It follows that cyanosis in warm areas depends much more on the content of reduced hæmoglobin in the arterial blood than in the venous blood It is extremely rare for the arterial oxygen saturation to fall below 85 per cent in these uncomplicated low output states

In view of these findings the term peripheral cyanosis has come to have a narrower meaning than that originally intended it may be defined as cyanosis of cold surfaces due to reduction of peripheral blood flow Thus it is seen chiefly in the skin of the fingers ears nose cheeks and outer side of the lips, it is not seen in the conjunctivæ palate or inner side of the lips or cheeks In heart failure with a low cardiac output considerable vasoconstriction occurs in certain territories in order to maintain the blood pressure the skin being relatively unimportant is one of these territories, and the vasoconstriction is most intense in exposed surfaces which are necessarily cooler The diminished blood flow leads to increased oxygen extraction by the tissues and the subpapillary venous plexuses of the skin must contain a high proportion of reduced hæmoglobin

At the bedside considerable difficulty may be experienced in attempting to distinguish between central and peripheral cyanosis Cyanosis of the conjunctivæ palate tongue and inner side of the lips and cheeks is always central In congenital heart disease cyanosis is certainly central if it is associated with clubbing and polycythæmia and probably central if it deepens on effort In suspected cor pulmonale cyanosis is surely central if associated with warm hands capillary pulsation digital throbbing distended forearm veins and a water hammer type of pulse all manifestations of peripheral vasodilatation Peripheral cyanosis is limited to the ears nose cheeks outer side of the lips hands feet and digits and these parts are cold Clubbing is not associated but polycythæmia may be present if the cardiac output has been low for a sufficient time If doubt still exists despite close attention to these details direct measurement of the arterial oxygen saturation is advised the critical distinguishing level being 85 per cent with normal hæmoglobin

## SYNCOPE

There are many causes of transient loss of consciousness and a complete list would include the causes of epilepsy coma concussion and asphyxia but syncope has come to mean transient loss of consciousness of sudden onset due to inadequacy of the cerebral blood flow As so defined syncope may be divided into cardiac vasomotor or vaso vagal cerebral and anoxic forms

### *Cardiac syncope*

Cardiac syncope occurs when the heart through some fault in itself or in its great vessels fails to maintain an adequate cerebral circulation These faults are listed for convenience as follows

1 Cardiac standstill—vagal inhibition
2 Ventricular asystole—Stokes Adams fit
3 Ventricular fibrillation
4 Ball valve thrombus or pedunculated myxoma

5 Aortic stenosis
6 Paroxysmal rhythm changes with extremely rapid ventricular rates
7 Massive pulmonary embolism
8 Cardiac compression from hæmopericardium
9 Low cardiac output states under certain conditions

The practical mechanism whereby the heart fails to fulfil its task varies according to the lesion

In *cardiac standstill ventricular asystole ventricular fibrillation ball valve thrombus* and *pedunculated myxoma* loss of consciousness is abrupt and without warning The attack may occur at any time while the patient is walking standing sitting or lying At first the patient is grey or white flaccid pulseless and motionless The heart sounds are inaudible but respirations may continue In about 10 to 15 seconds anoxic twitchings begin and may develop into convulsions if the attack lasts long enough If recovery does not occur within two minutes death usually results Cardiac and ventricular asystole usually recover well within that time commonly within 5 to 20 seconds but ventricular fibrillation is usually though not necessarily fatal Ball valve thrombus and pedunculated myxoma are rare Return to consciousness is abrupt and complete and is followed by a vivid flush hyper oxygenated blood being flung into a dilated vascular system (reactive hyperæmia)

Similar attacks of uncertain mechanism may occur in *aortic stenosis* As a rule however syncope in aortic stenosis is vasomotor the valve lesion acting merely as a predisposing factor or it is due to a low fixed cardiac output (*vide infra*)

Heart rates up to 200 per minute in *paroxysmal tachycardia* are usually well tolerated but syncope may result if the rate is much faster Speed of over 300 per minute have been recorded The heart has no time to fill or empty properly at these high rates and both cardiac output and blood pressure fall precipitously

*Massive pulmonary embolism* may cause syncope when more than two-thirds of the circulation is blocked The onset is sudden but rarely so abrupt as in the group just mentioned Moreover it may be preceded by pain or tightness in the chest The duration of unconsciousness is longer being usually measured in minutes or even hours Recovery is at first only partial extreme faintness persisting During the attack the patient is limp grey sweating and breathless The pulse is thready or imperceptible the heart sounds faint or inaudible the blood pressure low or unobtainable

Smaller pulmonary emboli insufficient seriously to embarrass the circulation occasionally cause reflex syncope Such reactions may be prevented by means of atropine Similar attacks may be encountered in cases of acute myocardial infarction These should not be regarded as examples of cardiac syncope for the mechanism is vasomotor

In view of these findings the term peripheral cyanosis has come to have a narrower meaning than that originally intended it may be defined as cyanosis of cold surfaces due to reduction of peripheral blood flow Thus it is seen chiefly in the skin of the fingers ears nose cheeks, and outer side of the lips, it is not seen in the conjunctivæ palate or inner side of the lips or cheeks In heart failure with a low cardiac output considerable vasoconstriction occurs in certain territories in order to maintain the blood pressure the skin being relatively unimportant is one of these territories and the vasoconstriction is most intense in exposed surfaces which are necessarily cooler The diminished blood flow leads to increased oxygen extraction by the tissues and the subpapillary venous plexuses of the skin must contain a high proportion of reduced hæmoglobin

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*Stimulation of other receptors that excite a vaso vagal reaction*

1 Psychogenic disturbances
2 Carotid sinus compression
3 Extreme pain
4 Cardiac infarction and other sudden visceral catastrophies

This list is by no means complete but it includes most of the common causes of vasomotor syncope

MECHANISM Syncope from hæmorrhage has been thoroughly investigated in blood donors As the blood volume diminishes the venous pressure falls and the cardiac output is reduced Compensatory vasoconstriction may temporarily maintain the blood pressure The faint, which is associated with a sudden fall in blood pressure and pronounced bradycardia appears to be due to sudden vasodilatation in muscle (Barcroft *et al* 1944) This vasodilatation is mediated by vasomotor nerves (Barcroft and Edholm 1944) Whether this reflex is excited by the fall in venous pressure or otherwise is unknown but it is clear that diminution in the blood volume is not directly responsible for the faint for the cardiac output may not alter at the critical moment – the peripheral resistance simply collapses

This sequence of events has also been demonstrated when syncope results from the prolonged application of venous tourniquets to the thighs and probably occurs in all cases of syncope initiated by a critical fall in central venous pressure (Sharpey Schafer 1944) Venous tourniquets on the thighs act as a bloodless venesection by trapping blood in the legs Fainting in soldiers on parade who may have to stand at attention for long periods is believed to depend on similar factors The fall in central venous pressure initiating orthostatic syncope following lumbo dorsal sympathectomy is due to abolition of veno motor tone in the lower half of the body Veno motor paralysis may also be partly responsible for fainting following the injection of ganglionic blocking agents Spontaneous toxic and convalescent ortho static syncope may also be due to loss of veno motor tone

Other forms of postural syncope include fainting in pregnant women when they lie on their backs too long and fainting in certain subjects on adopting the lordotic position The fall in central venous pressure is then attributed to compression of the inferior vena cava by a pregnant uterus or by the liver which is forced against the spine (Bull 1948)

*Syncope from chemical agents* which cause sudden profound vasodilatation is directly due to collapse of the peripheral resistance The blood pressure falls steeply but the cardiac output may be raised and there may be tachycardia instead of bradycardia Heat gross aortic incompetence and other vasodilatation states predispose to syncope by lowering the peripheral resistance

Loss of consciousness produced by the intravenous injection of acetyl choline *mecholin* (acetyl beta methylcholine) and *doryl* (carbo amino acetylcholine) is preceded by flushing and a feeling of warmth due to

vasodilatation and by sweating There is commonly abdominal colic nausea or vomiting and desire to micturate or defæcate The blood pressure is low but the pulse rate accelerates Patients may complain bitterly after regaining consciousness saying they feel dreadfully weak', as if they had been ill for months Ordinary therapeutic doses of mecholin and doryl rarely cause syncope the dose must be large and given intravenously Symptoms are relieved at once by 1 to 2 mg of atropine

Syncope from histamine nitrites and diodone is also preceded by flush ing headache and tachycardia Flush syncope may occur spontaneously in women at the menopause or in men at the climacteric Both hot flushes and syncope disappear following treatment with stilbœstrol 0 5 to 1 mg daily

Syncope is not uncommon in hypertensive subjects being treated with hexamethonium or ansolysen It is usually postural and may be severe There is not only collapse of the peripheral resistance but the central venous pressure falls blood being pooled in the periphery The patient should be laid on a couch and tilted head down by means of blocks under the foot end mephentermine 5 mg may be given intravenously and repeated when necessary or noradrenalin may be given by intravenous drip in a strength of 4 or 5 mg per litre the rate being governed by the blood pressure response

The severe collapse that sometimes follows the intravenous injection of too large a dose of quinidine is usually due to its vasodilating action but cardiac standstill or ventricular asystole is occasionally responsible Too large a dose of procaine amide may have a similar effect on the peripheral resistance

*The simple psychogenic faint* is initiated by emotional disturbance or by stimulation of the afferent component of a conditioned reflex, both result in a powerful autonomic discharge The type of emotion usually responsible is a mixture of fear amazement and curiosity as may arise when a nurse sees a thoracic paracentesis for the first time or when a hypersensitive subject witnesses a street accident The vasomotor centre appears to be suddenly depressed and there are associated cholinergic manifestations the chief result is gross vasodilatation This is certainly not in the skin which is pale and cold but may be in muscle or in the splanchnic bed The peri pheral resistance collapses and the blood pressure sinks rapidly As the cerebral blood flow depends chiefly upon the blood pressure it becomes inadequate and consciousness is lost Spontaneous recovery is inevitable for three reasons first, unconsciousness abolishes the trigger secondly liberated acetylcholine upon which many of the features of the attack may depend is rapidly destroyed by choline esterase thirdly the horizontal position naturally adopted by an unconscious subject increases the cardiac output and is favourable to the cerebral blood flow

*Carotid sinus syncope* is said to be of four main types which may be repro duced by carotid sinus compression (Weiss and Baker 1933 Ferris Capps

and Weiss 1935) First syncope may be due to cardiac standstill Second loss of consciousness may be associated with a gross fall of blood pressure and with marked slowing of the pulse rate If the latter is restored to normal by atropine consciousness is not regained if the blood pressure is restored by any means consciousness returns even though the pulse remains slow It is the low blood pressure and not the slow pulse rate which is responsible for the syncope This type corresponds to vaso vagal syncope Third carotid sinus pressure may induce syncope associated with a profound fall in blood pressure without slowing of the pulse rate It is doubtful if there is any fundamental difference between these two forms of attack, for not infrequently the first type merges into the second indeed it has been suggested that initial slowing of the heart occurs in all cases but that subsequent quickening resulting reflexly from the low blood pressure may occur so rapidly as to mislead the observer

Weiss and Baker describe a fourth type of syncope resulting from carotid sinus pressure in which the blood pressure and pulse rate are unchanged and refer to it as cerebral syncope This appears to be allied to epilepsy for no reduction of cerebral blood flow can be demonstrated

Spontaneous carotid sinus syncope may occur in rare instances The organ is hypersensitive and may be excited by sudden pressure of the neck against a tight collar The condition may be cured by carotid sinus denervation

Reflex syncope from pain myocardial infarction pulmonary embolism etc is similar in mechanism to the simple psychogenic faint

CLINICAL FEATURES Spontaneous vasomotor syncope is ushered in with numerous signs and symptoms of autonomic disturbance e g yawning pallor, sweating coldness of the skin a sinking feeling in the pit of the stomach general muscular weakness subjective changes of temperature a feeling as if the blood was all rushing downwards epigastric discomfort and nausea desire to micturate or defæcate a feeling of light headedness and so forth

Patients are aware of imminent loss of consciousness and although the onset of the faint may be described as quick or sudden it is never abrupt

Susceptible individuals faint when standing up rarely when sitting and practically never when lying they faint in company or when in reach of company, rarely when alone They are especially liable to attacks in closed spaces in church in the cinema and in circumstances that provoke emotional disturbance

The muscles are flaccid in vasomotor syncope so that the patient collapses like a house of cards his final position being determined by gravity he lies limp and inert in a sprawled or crumpled position and may well be on his back He is deathly white and often cold and clammy The eyes may be open or closed the position of the upper lid being governed by gravity The pupils are dilated and may be insensitive to light the reflexes and tendon jerks absent or depressed The tongue is never bitten but

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urine may be voided The essential feature is the low blood pressure which may be in the region of 50 or 60 mm Hg more often it cannot be determined The pulse rate is slow normal or quick In severe attacks slight twitching may be seen but is uncommon

The duration of vasomotor syncope is variable and though usually measured in minutes it may last much longer even up to an hour Consciousness is regained gradually and the patient then feels weak and ill he may complain of headache nausea or vomiting of a continued feeling of faintness or light headedness of trembling and shaking or of cold sweats He rarely recovers completely for half an hour or so and usually likes to lie down until he is better

Historically the chief difficulty is to distinguish vasomotor syncope from cardiac or cerebral syncope and from epilepsy

Meniere s syndrome or aural vertigo is usually recognised by its spinning quality but occasionally there is no spinning but merely unsteadiness imbalance or sudden attacks in which the subject is thrown violently forwards or backwards Consciousness is rarely lost however and either tinnitus or deafness is usually associated

*Cerebral syncope*

Cerebral syncope may result from cerebral vascular spasm or transient occlusion The fault is local

*Hyperventilation syncope* is the best example Forced breathing results in carbon dioxide washout with secondary alkalæmia Carbon dioxide ordinarily helps to maintain an adequate degree of cerebral vasodilatation (Norcross 1938) its lack causes cerebral vasoconstriction This induces dizziness within a minute in most normal individuals undergoing forced breathing If hyperventilation is maintained long enough syncope may occur Spontaneous attacks are seen in hysteria and sometimes in encephalitis lethargica There is usually associated vasoconstriction in the extremities with pallor cyanosis and tingling of the fingers and toes and there may be tetany The blood pressure is maintained or raised owing to vasoconstriction the latter tending to prevent reduction of cerebral blood flow

Forced breathing may be used as a test in cases of syncope to discover whether an attack can be reproduced It should be remembered however that epilepsy is sometimes excited by hyperventilation so that the diagnosis depends upon the nature of the induced attack not upon the simple fact that consciousness is lost The effects of spontaneous hyperventilation may be quickly abolished by the inhalation of carbon dioxide This may be accomplished by breathing in and out of a paper bag or long rubber tube

Loss of consciousness due to hypertensive encephalopathy or to cerebral vascular lesions with or without associated spasm of cerebral vessels is usually called coma unless convulsive epilepsy occurs Embolism however especially when due to air or fat may provoke an attack which fulfills the

definition of syncope The onset is abrupt and recovery may be remarkably quick and complete if the embolism moves on or if spasm passes off suddenly

Loss of consciousness occasionally occurs in Menière s syndrome but is then probably a vaso vagal reaction

Bilateral carotid compression an old ju jitsu trick is a most effective way of inducing unconsciousness in an adversary

*Anoxic syncope*

Loss of consciousness resulting from most causes of anoxia is described as asphyxia or coma Anoxic syncope however may occur in congenital heart disease with right to left shunt, especially in Fallot's tetralogy and is attributed to diminished peripheral resistance increased pulmonary resistance or a fall in total cardiac output A vaso vagal turn may have a disastrous effect in Fallot s tetralogy for the drop in blood pressure at once increases the amount of blood shunted from right to left and the sudden fall in arterial oxygen saturation may further depress the vasomotor centre so that a vicious circle is established patients may die in this way In four cases of anoxic syncope investigated by the writer however an increase of pulmonary resistance seemed to be responsible for the attacks Loss of consciousness was associated with extreme cyanosis disappearance of the characteristic pulmonary systolic thrill and murmur and no fall in blood pressure In one instance the arterial blood was almost completely un saturated Raising the blood pressure well above normal by means of methedrine had no effect on the arterial oxygen saturation and did not restore consciousness These cases behaved as if there were transient func tional pulmonary atresia whether the obstruction was due to temporary closure of the infundibulum itself or to pulmonary vasoconstriction could not be determined No structural block by a clot for example was found at necropsy in the case that died in the attack The writer has also witnessed syncope in Fallot s tetralogy resulting from an ill advised venesection since the blood pressure fell sharply however the increased cyanosis that accompanied loss of consciousness could well have been due to a vaso vagal mechanism and not to reduction of total cardiac output *per se*

*Tussive syncope* (from a prolonged attack of coughing) may be anoxic or asphyxial in one sense but is more properly ascribed to failure of cardiac filling due to an extremely high intrathoracic pressure which totally obstructs the venous return at the thoracic inlet

## *PALPITATIONS*

Palpitations may be rapid and regular with abrupt onset and offset as in paroxysmal tachycardia rapid and chaotic as in auricular fibrillation or fleeting and repetitive as with ectopic beats in such cases the abnormal rhythm can usually be recognised from the description of the sensation Palpitations may be heavy rather than fast or irregular however and then

an increased stroke volume may be responsible Physiological or pathological hyperkinetic circulatory states aortic or mitral incompetence patent ductus ventricular septal defect and atrial septal defect may cause heavy thudding of this kind In both types the sensation seems to be caused by a radical change in the natural stroke action of the heart it is the unusual movement of the heart within the thorax that is felt not an increased force of cardiac contraction nor more forcible valve closure Thus palpitations are not a feature of aortic stenosis or pulmonary stenosis nor of malignant hypertension or primary pulmonary hypertension The point may be further elaborated in respect of palpitations due to ectopic beats It is usually said that it is not the ectopic beat which is felt but the strong beat following the compensatory pause Anyone who has himself experienced ectopic palpitations is invited to question this He may well beg to disagree the quick beat out of time with the heart improperly filled gives rise to the first sensation and thus alone may be felt or it may be followed by a second sensation due to the beat of the over filled heart after the pause A run of ectopics makes it only too obvious that the quick beat is felt

A third type of throbbing is vascular This may be arterial as in aortic incompetence or venous as in gross tricuspid incompetence It is again the unusual movement within the tissues that is felt Tactile perceptors in the skin may be stimulated by pressure from within as can be demonstrated easily enough during the passage of a venous catheter for this procedure causes no sensation at all unless the catheter tip comes into indirect contact with the skin in the arm neck or thorax

Patients may also complain of a beat in the head which is really a sound It may be single an internal phase III Korotkow sound associated with vasodilatation or it may be double when both first and second heart sounds are heard The symptom usually occurs in bed at night

Palpitations of any kind naturally draw the patient s attention to his heart and he may soon begin to question its integrity this leads to anxiety and since emotional turmoil is the commonest cause of the symptom at once closes a vicious circle

## *HÆMOPTYSIS*

Although hæmoptysis may occur in a wide variety of cardiovascular diseases it only does so under strictly defined circumstances

(1) A necrotic arterial lesion may rupture, as in disseminated lupus Pulmonary tuberculosis may accidentally complicate any form of heart disease this accounted for hæmoptysis in two out of three cases of A S D in the writer s series in which this symptom occurred (2 per cent) An arterio venous aneurysm may rupture or a syphilitic or mycotic aneurysm may rupture into the bronchus Pulmonary lesions like bronchiectasis or bronchial carcinoma should not be overlooked when hæmoptysis occurs unexpectedly in association with heart disease All these hæmorrhages are essentially necrotic

(2) Hæmoptysis may occur suddenly as the first symptom of mitral stenosis and may be precipitated by effort or pregnancy This kind of pulmonary apoplexy has been attributed to rupture of small pulmonary or broncho pulmonary anastomotic venules as a result of a sudden rise of left atrial pressure Such hæmorrhages tend to cease as the pulmonary veins thicken in response to the rise of pressure within them, or when the pulmonary vascular resistance exceeds 10 units (800 dynes sec /cm 5) and so protects the pulmonary venous system from developing too high a pressure (Wood 1954)

(3) Bloodstained sputum may accompany an attack of paroxysmal cardiac dyspnœa in mitral stenosis or left ventricular failure and may be attributed to intense pulmonary venous congestion (congestive hæmoptysis) In these cases the dyspnœa is much more important than the hæmoptysis Blood-spitting in an attack of bronchitis complicating mitral stenosis has a similar significance and the pink frothy sputum of acute pulmonary œdema is closely related

(4) Frank hæmoptysis may be caused by pulmonary infarction This is usually a late manifestation of heart disease for the phlebothrombosis in the legs from which the responsible embolus springs is apt to be a complication of congestive heart failure proper Emboli from right sided bacterial endocarditis may also cause hæmoptysis from small areas of infarction

Hæmoptysis rarely if ever results from uncomplicated pulmonary plethora in patent ductus V S D and A S D nor is it a symptom of pulmonary hypertension primary secondary or hyperkinetic It may occur with passive pulmonary hypertension but here it is the high pulmonary venous pressure that matters not the arterial

Hæmoptysis in essential hypertension is sometimes due to posterior epistaxis in other cases however this can be excluded and the site of the hæmorrhage is then a matter for conjecture It is not common

## *RECURRENT BRONCHITIS*

Trivial upper respiratory tract infections may rapidly develop into florid bronchitis in two main types of disturbed physiology in cardiovascular disease pulmonary plethora and pulmonary venous congestion

Pulmonary plethora i e an increased pulmonary blood flow occurs typically in patent ductus and ventricular or atrial septal defect pulmonary venous congestion in left ventricular failure and mitral valve disease It is suggested that the violent reaction to trivial infection is due to the hyperæmic state of the pulmonary circulation Most diseases require both an etiological agent and some tissue reaction a pathogenic agent may be harmless Thus spirochætal aortitis does not occur in syphilis although the aorta may contain numerous spirochætes

there is no tissue reaction again amœbæ do not necessarily cause dysentery when they take up their abode in the human colon but only when reactive ulcerative colitis develops Hyperæmia is one of the fundamental reactions to infective agents and a major part of what is known as inflammation if the lung is already hyperæmic an inflammatory reaction would be expected to be intense

Recurrent bronchitis is not a feature of pulmonary ischæmia in congenital anomalies with right to left shunt or in low output states for example it is uncommon in Fallot s tetralogy and primary pulmonary hypertension

Recurrent bronchitis is of course an important feature of anoxic cor pulmonale but here it has a causal role

Both chronic cough and bronchitis may also result from compression of the right or left main bronchus from aneurysm of the aorta or pulmonary artery or from aneurysmal dilatation of the left atrium

## *INSOMNIA*

Many patients with heart failure complain bitterly of insomnia Since the physiology of sleep is still improperly understood little would be gained by discussing the mechanism of the insomnia But there are two obvious symptoms which may interrupt sleep in cases of heart failure—paroxysmal cardiac dyspnœa and Cheyne Stokes breathing

Nocturnal dyspnœa in left ventricular failure and mitral valve disease may be abolished by means of a low sodium diet and mercurial diuretics and it has been well said that the best cure for insomnia in these cases is mersalyl (Evans)

Cheyne Stokes breathing tends to wake the patient during the dyspnœic phase of each respiratory cycle The symptom can be very troublesome because it is aggravated by morphine barbiturates and indeed by sleep itself Fortunately however it can usually be abolished by aminophylline preferably given as a suppository in a dose of 0 4 G at night Aminophylline has the double advantage of preventing paroxysmal cardiac dyspnœa as well

Thus although barbiturates may have to be used for the insomnia of heart failure better results are usually achieved by the efficient treatment of the heart failure itself

## *SYSTEMIC EMBOLISM*

Under certain circumstances a clot may form in the left side of the heart or in a pulmonary vein and if liberated must find its way into some cerebral visceral or peripheral artery The chief causes of thrombosis in the cavity of the left ventricle are cardiac infarction and isolated myocarditis in the left atrium mitral valve disease and auricular fibrillation and in the aortic or mitral valve bacterial endocarditis The commonest cause of embolism is undoubtedly mitral valve disease with auricular fibrillation

There is increasing evidence that only a fresh clot is liable to be set free and that in mitral valve disease this fresh clot is most likely to form within the first few days of the onset of uncontrolled auricular fibrillation whether paroxysmal or permanent The embolism may occur while the auricle is still fibrillating or soon after normal rhythm is resumed spontaneously or in response to quinidine therapy

*Cerebral embolism*

The clinical features of cerebral embolism differ from those of cerebral thrombosis in three ways first the attack is abrupt rather than sudden in onset often with loss of consciousness second the symptoms are maximal at the start and third remarkable recovery may take place within a few minutes or hours In addition one of the known underlying causes of systemic embolism should be apparent

Treatment consists of doing everything possible to promote an effective cerebral circulation and to prevent secondary thrombosis The patient should be nursed flat if the state of the heart allows it Uncontrolled auricular fibrillation and congestive heart failure should be treated quickly and efficiently to encourage the maximum cardiac output Oxygen with 5 per cent carbon dioxide may be inhaled with advantage and the blood pressure must be maintained if necessary by means of a noradrenaline intravenous infusion at a rate of approximately 10 $\mu$g per minute mephentermine (wyamine) 35 mg intramuscularly or some other pressor amine for the cerebral blood flow depends chiefly upon the arterial carbon dioxide content and the blood pressure Vasodilators (to relieve vascular spasm) are not recommended for they are more likely to act peripherally than on the cerebral vessels and by lowering the blood pressure may have an adverse effect on cerebral flow Anticoagulants have often been withheld on the grounds that they might induce hæmorrhage in an area of cerebral softening but there is little factual evidence to support this view and in the writer s opinion they should be given both to prevent secondary thrombosis and further embolism

*Visceral embolism*

An embolus may lodge in a mesenteric splenic renal coronary or other visceral artery

*Mesenteric embolism* is characterised by sudden severe epigastric pain with or without shock The patient presents with an acute abdomen but on examination there is no guarding and but little tenderness Within a few hours malena appears the blood being dark red in colour Symptoms and signs of sub acute or complete intestinal paralysis follow with vomiting and increasing distension The outlook is bad in the more severe cases death occurring in a few days In less severe cases however despite evidence of ileus and even though malena may be extensive recovery may occur within the week

there is no tissue reaction, again, amoebae do not necessarily cause dysentery when they take up their abode in the human colon, but only when reactive ulcerative colitis develops. Hyperaemia is one of the fundamental reactions to infective agents and a major part of what is known as inflammation. If the lung is already hyperaemic an inflammatory reaction would be expected to be in excess.

Recurrent bronchitis is not a feature of pulmonary oligaemia in congenital anomalies with right to left shunt or in low output states. For example, it is uncommon in Fallot's tetralogy and primary pulmonary hypertension.

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## *SYSTEMIC EMBOLISM*

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usually established by the deep femoral artery When collateral vessels are atherosclerotic or otherwise diseased however as is common in the aged, these principles do not apply for then a relatively small embolism may precipitate gangrene Each case must be considered carefully on its merits Pain is due to ischæmia of working muscle in the affected territory Thus an embolus may lodge quietly in a resting limb and cause no pain until the limb is actively moved If there is sufficient ischæmia of nervous tissue pain at rest paræsthesia or peripheral anæsthesia may be present On examination the affected limb is colder than its fellow and may be pale or cyanosed The distal vessels are impalpable Methodical palpation of the vessels in a proximal direction may reveal the site of the embolism for above it pulsation is normal

The problem in every case is whether to advise embolectomy or con servative treatment Good judgment would take into account the site of the embolus the age of the patient the presence or absence of peripheral vascular disease such as atherosclerosis the objective findings concerning the immediate state of the peripheral circulation and the fact that if an operation is to be performed it should not be delayed more than six hours There are three other points of peculiar importance which should also be considered First an embolus often moves on from a position of danger to one of safety It is not wise to attempt to milk it down the limb because the embolus may then break up and its fragments may block several distal vessels and so interfere seriously with collateral circulatory efficiency Second there may be considerable vascular spasm associated with an embolus so that initial ischæmia may be disproportionate to the size of the vessel blocked Third in cases associated with heart failure and auricular fibrillation with rapid ventricular rate an inadequate collateral circulation may be made sufficient by improving the cardiac output Dramatic effects may be obtained in such cases by intravenous digoxin or strophanthin when a critical situation may be turned within half an hour

The fact is that most of these cases do better than is generally supposed The wisest course is to start intensive medical treatment immediately the diagnosis is made Morphine or pethidine heating the body with an elec tric cradle or hot water bottles and various vasodilators such as eupaverine or priscol are helpful Hypertonic saline is rarely practical in cardiac cases If after two hours of such treatment the peripheral circulation as judged by the colour temperature and function of the limb remains in jeopardy the surgeon should be invited to perform embolectomy Once this decision has been made the physician should increase rather than decrease his efforts to make the operation unnecessary and in close co operation with the surgeon should be prepared to ask for a little more time if there is any sign of improvement A good surgeon however will be anxious to avoid delay if in his own opinion conservative measures are proving ineffective

Reluctance to advise embolectomy is based on three precepts first if an operation is to be performed heparin may have to be withheld

anticoagulants are highly desirable to prevent post embolic thrombosis and further embolism second it is embarrassing to witness exposure of a vessel which is found to be pulsating freely by the time it is reached third, arteriotomy is not devoid of the risk of post operative thrombosis Nevertheless embolectomy is essential if the limb is really in danger

## *OTHER SYMPTOMS*

*Pulmonary embolism* usually secondary to phlebothrombosis in the legs is a common complication of heart failure with a low cardiac output and is discussed fully in Chapter XVII

*Cardiac cachexia* sometimes obscured by œdema and swelling of the abdomen is a common late manifestation of chronic heart failure It occurs especially in lingering cases of aortic, mitral or tricuspid stenosis

*Cerebral symptoms* include varying grades of dementia in advanced hypertension attacks of encephalopathy in malignant hypertension and confusional or frankly psychotic states attributed to anoxia diminished cerebral blood flow or impaired hepatic function as for example in cor pulmonale following operations on the heart in which the blood pressure has dropped to low levels for too long a period and in severe low-output heart failure respectively

*Swelling of the abdomen* due to gross enlargement of the liver with or without ascites may complicate chronic heart failure from any cause but is seen especially in constrictive pericarditis severe tricuspid stenosis and advanced cases of functional tricuspid incompetence associated with chronic right ventricular failure Cirrhosis of the liver in alcoholics with heart failure may provide independent grounds for ascites and thrombosis of the hepatic vein may complicate heart failure

*Jaundice and vomiting* complicating heart failure are discussed in Chapter VII

*Oligemia and nocturia* are also discussed under Heart Failure and nocturia again in the chapter on Hypertension

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CHAPTER II

# PHYSICAL SIGNS

THERE are two methods of examining a patient the first begins at the top of the head and ends with the toes a method often adopted for the sake of convenience the second is to examine the various systems of the body one by one in logical sequence The procedure recommended here is concerned only with the cardiovascular system but it is essential of course that all other systems be examined

## GENERAL INSPECTION

While extracting the history the physician should be making a preliminary general inspection He should pay particular attention to the head and neck looking for goitre and for the eye signs of thyrotoxicosis for Corrigan s sign and especially for jugular pulsation He will note the general build and appearance of the patient his attitude and demeanour and should form some idea of his character He should observe plethora, pallor or cyanosis He may see that respiration is hurried irregular shallow or wheezy or he may detect the tell tale sigh of emotional tension He is sure to glance at the hands noting their posture shape colour and behaviour he may discern clubbing of the fingers spooning of the nails tremor or palmar sweating All these things and many others he will learn to observe without effort taking note of them without seeming to do so, and in such a limited survey may be put on the track of the correct diagnosis and be forewarned where to look most diligently for further signs

## THE ARTERIAL PULSE

It is customary to examine the pulse first at the wrist and to consider it in terms of speed rhythm tension amplitude and quality at the same time it is convenient to note the state of the arterial wall Whilst speed and rhythm may be checked by auscultation of the heart and tension by sphygmomanometry the quality and amplitude of the pulse wave can only be analysed in peripheral vessels and are features of great diagnostic importance

The most convenient and revealing pulse to examine is the right brachial it is best felt with the thumb of the right hand, the physician being on the patient s right side The quality of the brachial pulse can only be learned by experience What is felt is a pressure wave, and to appreciate it fully it is necessary to vary the pressure which the thumb exerts upon the artery until maximum movement is detected This implies exerting a force equal

to the diastolic arterial pressure The upstroke of the pulse or percussion wave is smooth and fairly sharp without being abrupt and occupies about 0 08 sec (range 0 06 to 1 0 sec) the peak of the wave is momentarily sustained, so that arterial pressure curves have a rounded summit occupying 0 06 to 0 12 sec and the downstroke is initially fairly quick but not precipitous, the whole movement being smooth and uniform (fig 2 01)

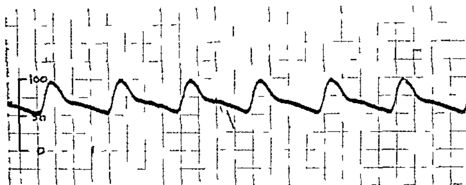



Fig 2 01—Normal arterial pulse in a child

*Pulsus parvus*

A pulse wave of small amplitude means that systolic and diastolic pressures are nearer one another than usual i e they are approaching the mean arterial pressure This is a sign of vasoconstriction and generally implies a low cardiac output In normal subjects it may be due to cold or anxiety It occurs locally in the arteries of the legs in coarctation of the

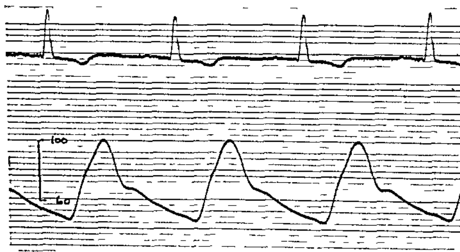



Fig 2 02—The anacrotic pulse of aortic stenosis the percussion wave is dwarfed occupies 0 1 second the large blunt peak builds up slowly the maximum pressure being reached until 0 24 second after the onset (major time intervals 0 1 sec)

aorta and in any artery distal to partial occlusion. In disease it is characteristic of severe hypertension aortic stenosis cardiac infarction mitral stenosis extreme pulmonary hypertension severe pulmonary stenosis, tricuspid stenosis Pick s disease pericardial effusion myocarditis and any form of low output failure

*Bounding pulse*

A large pulse wave of good form means a high pulse pressure associated with an increased blood flow and is seen characteristically in the hyperkinetic circulatory states

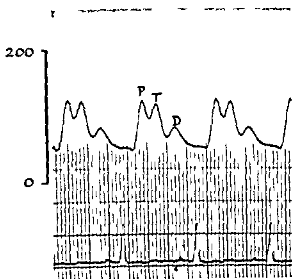



Fig 2 03—Pulsus bisferiens external arteriogram showing two peaks in systole P being the percussion wave and T the tidal wave they are followed by the dicrotic wave

*Anacrotic pulse*

A slow upstroke associated with a pulse wave of low amplitude is typical of aortic stenosis (fig 2 02) Sometimes a notch can be felt on the upstroke this is the *anacrotic* pulse (or in full anadicrotic—ανα up δις twice κροτος beat)

*Pulsus bisferiens*

In combined aortic stenosis and incompetence a double beat during systole may be very pronounced (fig 2 03) it shows up well in the ordinary external arteriogram when some pressure is applied to the surface of the artery by means of the pick up device but the trough between the two peaks usually disappears in intra arterial pressure tracings being replaced by a short plateau or shoulder (fig 2 04) The second component of the beat has been attributed to a tidal wave the onset of the percussion wave being reflected back from the periphery before the tail of the percussion wave has passed the meeting of the two having a summation effect (Bramwell 1947)

*Dicrotic pulse*

In the better known form of twice beating pulse the percussion wave is followed by a palpable secondary wave after aortic valve closure (fig 2 05) In normal individuals the downstroke of the pulse wave is interrupted by a notch (dicrotic notch) representing aortic valve closure but the sma positive pressure wave (dicrotic wave) that follows the notch or distorts

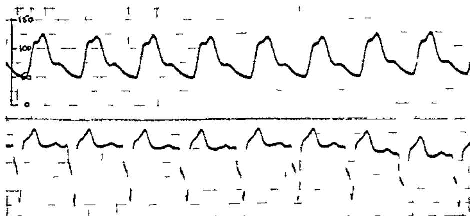



Fig 2 04—Intra arterial pressure tracing of the pulsus bisferiens The dip between percussion and tidal waves is replaced by a plateau




Fig. 2 05—Intra arterial pressure tracing of a typical dicrotic pulse (D)

the contour of the descent cannot be felt clinically The dicrotic pulse is encountered chiefly in patients sick with some fever such as typhoid the peripheral resistance is low the blood pressure low, the arteries lax and the cardiac output probably normal

*Water hammer pulse*

This aptly describes the combination of an abrupt percussion wave ill sustained crest, and rapid collapse (fig 2 06) *A water hammer is a hermetically sealed tube containing a vacuum partly filled with water* when the tube is inverted quickly the water drops abruptly and imparts a palpable shock to that end of the container A pulse having this charac teristic quality indicates a low filling resistance in the reservoir into which the left ventricle pumps its contents In health a low resistance is always peripheral and means vasodilatation usually due to heat exercise emotional disturbance pregnancy or alcohol Peripheral vasodilatation is characteristic of the hyperkinetic circulatory states such as thyrotoxicosis anæmia beri beri, hepatic failure and anoxic cor pulmonale Peripheral resistance is lowered by a leak in the arterial side of the circulation e

in arterio venous fistula patent ductus aortic incompetence mitral incompetence and possibly ventricular septal defect The physiological counterpart of an arterio venous fistula may also occur in the thyroid gland in thyrotoxicosis (spontaneously or as a result of anti thyroid drugs) in the uterus during pregnancy and in bone in Paget s disease Again peripheral

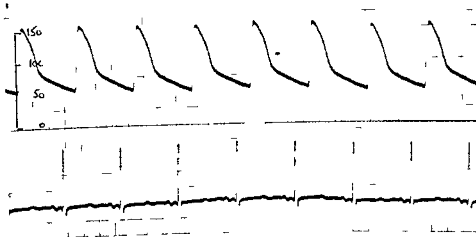



Fig 2 06—Intra arterial pressure tracing of a water hammer pulse in a case of patent ductus arteriosus Note the singularly abrupt wave front

vasodilatation tends to accompany most of the conditions mentioned with the teleological effect of encouraging forward flow in competition with the leak Finally a water hammer pulse often accompanies complete heart block, in which an unusually large volume of blood is flung into a relatively empty arterial reservoir each beat

The amplitude of the water hammer pulse varies considerably in these different conditions being highest in aortic incompetence, heart block and the hyperkinetic circulatory states (physiological or pathological) and lowest in mitral incompetence The collapse occurs in the latter part of systole and the dicrotic notch is usually displaced towards the base line In the majority the systolic blood pressure is somewhat raised and the diastolic low

*Pulsus alternans*

Alternate larger and smaller beats with normal rhythm are characteristic of severe systemic hypertension or left ventricular failure The mechanism is discussed in Chapter VII Similar alternation may occur in the pulmonary arterial pulse right ventricle and right atrium in severe pulmonary hypertension or stenosis (fig 2 07) There is no change in alternate electrocardiographic complexes and as a rule the phenomenon cannot be recognised by means of auscultation A bout of alternation is frequently precipitated by an ectopic beat in susceptible cases

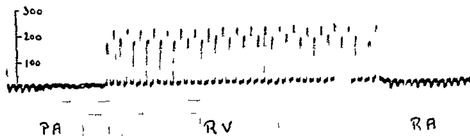



Fig 2 07—Right ventricular alteration in a case of severe pulmonary stenosis (Paper speed - 5 mm per sec)

*Pulsus paradoxus*

The pulse normally quickens during inspiration and slows during expiration but it does not alter appreciably in volume in chronic constrictive pericarditis and in tense pericardial effusion however it may become very small or disappear altogether during inspiration The mechanism is discussed in Chapter XIII

*Pulsus bigeminus*

Alternate ventricular ectopic beats results in coupling each pair of beats consisting of a normal or large pulse followed by a small one

*The pulse in other arteries*

The pulse should be checked in all the palpable major arteries on both sides i e in the radials brachials carotids femorals popliteals posterior tibials and dorsal arteries of the feet

*Difficulty in locating the radial artery* may be due to its taking an aberrant dorso lateral course *Weakness on one or other side* usually denotes proximal compression as from aneurysm of the aorta but a weak left radial pulse may be due to an ectopic origin and aberrant course of the left subclavian artery

The carotids may present an unusual degree of pulsation associated with coarctation of the aorta Corrigan s sign of aortic incompetence kinking from atherosclerosis or a thrill or shudder indicating aortic stenosis

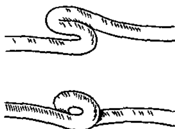


Fig 2 08—Two types of kinked carotid

CORRIGAN S SIGN consists of abrupt distension and quick collapse of the carotids the movement being of high amplitude It is discovered by inspection (Corrigan 1832) not by palpation and should not strictly be confused with a palpable water hammer pulse

CAROTID KINKING superficially resembles a rounded pulsating aneurysm

at the base of the right common carotid A short segment of the vessel is looped back sharply on itself to give this impression (fig 2 08) It is caused by elevation of the aortic arch as a result of hypertension or atherosclerosis so that the carotids, particularly the right come to be too long for the distance they occupy The lesion is seen especially in obese women in whom the heart is also elevated

Routine palpation of the arteries in the legs would insure the immediate recognition of coarctation of the aorta in nearly all cases *diminished and delayed femoral pulsation* being characteristic and almost pathognomonic The presence of pulsation in the vessels of the feet should always be recorded if only for subsequent reference

## THE EXTREMITIES

Further information of the kind partly given by the arterial pulse may be obtained from examining the extremities particularly the fingers hands and forearms

### *Signs of vasodilatation*

DIGITAL THROBBING indicates vasodilatation and may be detected by picking up all the fingers of the patient s right hand with all the fingers of the examiner s right hand so that the two sets grip each other gently finger to finger in a flexed position

CAPILLARY PULSATION has a similar significance and is best demonstrated by transilluminating the tip of the middle finger or thumb by pressing a pocket torch into the pad underneath and shading the nail bed from daylight with the flexed fingers of the examiner s other hand

WARM HANDS are associated with these signs of vasodilatation and if the blood flow is increased *the forearm veins are usually distended*

Vasodilatation occurs in all the physiological and pathological hyperkinetic circulatory states and in all conditions which may give rise to the water hammer pulse

### *Signs of vasoconstriction*

COLD HANDS are associated with peripheral vasoconstriction and when the blood flow is diminished the *forearm veins become spidery* Peripheral vasoconstriction may be due to cold when it helps to prevent loss of heat from exposed surfaces to apprehension as part of a general response or to a low cardiac output when it helps to maintain the blood pressure

### *Other circulatory signs*

THE COLOUR OF THE HANDS gives less information concerning blood flow and arterial tone As a general rule the colour is pink when there is vasodilatation and pale or blue when there is vasoconstriction But the palms of the hands may be bright red in certain cases of low output heart failure when hepatic function is sufficiently disturbed and the hands are pale in

anæmia and blue in anoxic cor pulmonale although the cardiac output may be high and the arterioles dilated Richly coloured often cyanosed hands are seen in polycythæmia vera

DIFFERENTIAL CYANOSIS between the hands and feet the hands being pink and the feet blue is pathognomonic of pulmonary hypertension with right to left shunt via a patent ductus arteriosus

THE RAYNAUD PHENOMENON (Raynaud 1862) defined by Hunt (1936) as intermittent pallor or cyanosis of the extremities precipitated by exposure to cold without blockage of the large peripheral vessels and with nutritional lesions if present at all limited to the skin cannot be described here in detail It must be stated however that at least one third of patients with myxœdema suffer from this disorder and that it is not infrequently the first symptom of the disease Hypersensitivity to cold and a reduced peripheral blood flow are presumably responsible Raynaud s phenomenon is not uncommon in other low output states such as hypertensive heart failure and advanced mitral stenosis on the other hand it is rare in thyrotoxicosis and other hyperkinetic circulatory states

THE SCLERODERMA OF THE FINGERS (acrosclerosis) that may be associated with Raynaud s disease is usually regarded as a vasomotor trophic change but may be associated with more widespread lesions particularly in the skin of the face and neck and in the submucosal connective tissue of the mouth and œsophagus (Olsen O Leary and Kirklin 1945) Scleroderma however may also involve the heart (Weiss *et al* 1943) In the majority of such cases the extremities have shown pigmentation a rheumatoid type of arthritis and Raynaud s syndrome in addition to the smooth glossy drum tight skin of scleroderma (fig 2 09)



Fig 2 09—Sclerodactyly

*Changes in the nails*

CLUBBING OF THE FINGERS AND TOES may occur in cyanotic forms of congenital heart disease bacterial endocarditis and anoxic cor pulmonale also of course in suppurative lesions of the lungs such as pulmonary abscess and bronchiectasis and bronchial carcinoma clubbing may also be hereditary, and has been reported in association with sprue cirrhosis of the liver, post operative myxœdema and syphilitic aneurysm (where it may be unilateral) Advanced clubbing is obvious the tips of the digits beyond the root of the nail being swollen rounded and congested there being an overgrowth of the soft tissues of the nail bed and hyperæmia The best sign of mild clubbing is probably obliteration of the normal angle between the base of the nail and the skin proximal to it (fig 2 10) Clubbing is rare in infancy even when cyanosis is intense but is common enough in Fallot s tetralogy by the age of two or three It may develop very quickly under appropriate circumstances *in two to three weeks for example* in cases of pulmonary abscess and may disappear equally quickly when its cause is radically removed e g when the arterial oxygen saturation is restored to normal by means of pulmonary valvotomy or infundibular resection in cases of Fallot s tetralogy The precise cause of clubbing is still unknown but it appears to be related to an increase of blood flow in the terminal digits (Mendlowitz 1938)

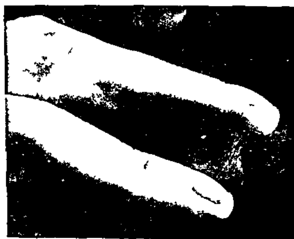


Fig 2 10—Clubbed fingers showing disappearance of the normal angle between the skin and nail

KOILONYCHIA (spooning of the nails) is a well known sign of iron deficiency anæmia the nails are flattened even concave fragile and tend to split longitudinally (fig 2 11) They are rapidly restored to normal as the anæmia improves with iron therapy Koilonychia has also been reported

thyro oxicosis without anæmia (Cocke and Luts 1944) and in some
es encountered in apparently normal individuals

OPAQUE WHITE NAILS have been reported in hepatic cirrhosis (Terry
54) including cardiac cirrhosis



Fig 2 11—Koilonychia The spoon shaped nails are holding a drop of water

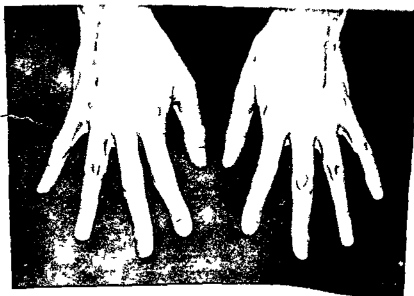


Fig 2 12—Arachnodactyly

*Congenital deformities*

ARACHNODACTYLY or spider fingers (fig 2 12) first described by Marfan (1896) is an hereditary and familial disorder of mesoblastic growth and in its complete form is characterised by elongated spidery fingers and toes thin facies tall lean build muscular hypotonia (and its consequences, e g scoliosis and flat feet) dislocation of the lenses high arched palate, deformed teeth and pigeon chest (Rados 1942) Cardiac anomalies, especially hypoplasia of the aorta (with or without dilatation aneurysm dissection or rupture) and atrial septal defect are associated in 40 to 45 per cent of cases and patients have an increased liability to rheumatism and rheumatic mitral or aortic valve disease (Reynolds 1950 Goyette and Palmer 1953)

SYNDACTYLY and POLYDACTYLY may also be hereditary or familial and may be associated with congenital heart disease

*Arthritis of the hands and feet*

RHEUMATIC FEVER in adults not infrequently attacks the small joints of the hands and may be mistaken for rheumatoid

RHEUMATOID itself may cause pericarditis with or without effusion

Historical or objective evidence of previous *gout* should be noted partly because in susceptible individuals an attack may be readily provoked by dehydration resulting from mercurial diuretics or a strict low sodium regime unless special precautions are taken

PULMONARY OSTEOARTHROPATHY associated with central cyanosis and an increased blood flow to the extremities is an uncommon complication of advanced anoxic cor pulmonale (see Chapter XVIII) The wrists elbows ankles and knees may all be involved as well as the small joints of the hands and feet

Heberden s nodes or other evidence of osteoarthritis are of no cardio vascular significance

*Nodes*

OSLER S NODES are small tender erythematous transient and often palpable skin lesions characteristic of bacterial endocarditis They occur especially in the pads of the fingers or toes the palms of the hands or soles of the feet and are due to infected emboli (Osler 1909)

RED TENDER MACULES biopsies of which may also yield positive cultures are equally if not more common in bacterial endocarditis

LARGER INFLAMMATORY NODES resembling a septic finger in the pre suppurative stage constitute a third type of peripheral lesion in this disease

DISSEMINATED LUPUS may give ri e to painful erythematous or hæmorrhagic necrotic nodes in the extremities (and elsewhere)

ERYTHEMA NODOSUM in the legs or forearms is too well known to warrant description (fig 2 13) It seems to be a non specific allergic type of tissue re action to a variety of antigenic agents including tuberculosis meningococcal

septicæmia streptococcal infection and a host of drugs particularly sulphathiazol It is not uncommon in sarcoidosis and is sometimes associated with rheumatic fever Not infrequently none of these agents or relationships can be demonstrated with certainty



Fig 2 13—Typical distribution of erythema nodosum

RHEUMATIC NODULES are illustrated and discussed in Chapter IX Similar and larger nodules may occur in rheumatoid arthritis

Heberden s nodes and chalky deposits of gout have already been mentioned

SPIDER NÆVI are not nodes but may be mentioned here for convenience They are characteristic of advanced disease of the liver and are usuall associated with bright red palms and other evidence of vasodilatation (see Chapter XX)

A GLOMUS TUMOUR is a minute subcutaneous erythematous or bluish point usually *under a nail and often exquisitely painful It is mentioned* here because it may be mistaken for an Osler s node It is essentially a small innocent tumour of one of the rounded arterio venous shunt arrangements known as glomera (*glomus*, a ball) which are so numerous in the tips of the fingers and palms

*Nervous disorders*

MOIST PALMS provide good evidence of an anxiety state

TREMOR should be interpreted with care Thyrotoxic tremor is fine regular, and constant The tremor of an ar cuff was designed for an irregular and inconstant-d arm e tremor applied to a large arm or thigh

ans disseminated sclerosis, fatigue or senility occasionally it is con
Congenital

ARALYTANY of the hands is commonly due to hysterical hyperventilation (1896) which causes tissue alkalæmia it is quickly relieved by the inhalation of in its carbon dioxide The sign is valuable when it is clinically uncertain whether thin overbreathing is due to pulmonary or cardiac disease or to hysteria A e g en ous tourniquet applied to the limb will augment carpal spasm (Trousseau's sign) or tapping the facial nerve with the finger may cause an obvious facial twitch (Chvostek's sign)

PERIPHERAL NEURITIS with motor weakness impairment of sensation and loss of tendon jerks may give the clue to the nature of an obscure cardiopathy such as periarteritis beri beri and diphtheria The signs of neurosyphilis may disclose the cause of aortic incompetence or a mediastinal mass signs of subacute combined degeneration of the cord may at once explain a hyperkinetic circulatory state transient paraplegia immediately distinguishes dissecting aneurysm from coronary thrombosis evidence of poliomyelitis however slight may reveal the true nature of a myocarditis

*Pigmentation*

Brownish pigmentation of the skin may be due to Addison's disease hæmochromatosis or scleroderma

*Loss of hair*

Loss of axillary hair is characteristic of hæmochromatosis

A host of other signs may be found in the extremities but most of those which have a bearing on the cardiovascular system have been mentioned and underline the importance of examining the hands and feet very closely

## THE BLOOD PRESSURE

The blood pressure was first measured directly in a live mare by Stephen Hales (1733) a brass pipe 1/6th of an inch in diameter was inserted into the left crural artery and connected to a vertical glass tube, blood rose in the tube to a height of 8 feet 3 inches above the level of the left ventricle

An excellent detailed account of the subsequent history of sphygmomanometry may be found in a monograph by Master Garfield and Walters (1952)

*Technique of measurement*

CLINICAL ESTIMATION Approximate estimation of the blood pressure by clinical means is not only possible but should be practised regularly, with experience it is easy to tell whether it is low normal or high and the procedure takes but a moment The physician should stand in front and to the right of the patient and should compress the right brachial artery (fig 2 13) while feeling the right radial pulse with the fingers ... ed to obl... the pulse represents the

systolic blood pressure The alternative method of placing three fingers on the radial artery the first to compress the vessel above the second to feel the pulse and the third to obliterate the ulnar collateral below is both difficult and cumbersome

SPHYGMOMANOMETRY In cardiovascular work however the blood pressure should always be measured with a mercurial manometer or reliable aneroid instrument The patient must be comfortable whether lying or sitting and must have had time to recover from any recent excitement or exertion The arm should be bared to the shoulder to avoid constriction from clothing and to facilitate proper application of the cuff The latter should be fitted closely and evenly round the arm so that r' lower edge is one inch above the bend of the elbow and the middle of the rubber bag lies over the brachial artery Preliminary readings should be taken by palpation the cuff is inflated rapidly until the brachial pulse is obliterated and is then deflated slowly the point at which the brachial pulse first reappears represents the systolic pressure as the cuff is further deflated brachial pulsation gradually assumes a water hammer quality and then abruptly resumes its normal character the reading corresponding to this sudden change represents the diastolic blood pressure When approaching an end point the pressure must be altered slowly in the cuff The palpatory method avoids the pitfall of the auscultatory gap and is uninfluenced by subjective auditory defects nevertheless it should be checked by auscultation The stethoscope should be applied lightly and accurately over the brachial artery just below but not in contact with the cuff The latter is then inflated to a pressure of some 30 mm Hg above the systolic pressure as found by palpation and slowly deflated The accepted systolic blood pressure is the highest level at which successive sounds (phase I of Korotkow) are heard As the pressure is further lowered in the cuff the dull thud of the upper limits is replaced first by a murmur (phase II of Korotkow) and then by louder and sharper sounds (phase III) the point at which these slapping sounds suddenly become muffled (phase IV) is usually taken as the diastolic pressure When there is vasodilatation especially when associated with aortic incompetence sounds may still be heard when the cuff pressure is reduced to zero but normally they disappear a few mm Hg below the change over

*The above recommendations are freely borrowed from the joint report of* the committees appointed by the British Cardiac Society and the American Heart Association for the standardisation of methods of measuring the arterial blood pressure (1939)

SIZE OF THE CUFF The cuff method of measuring the blood pressure is not entirely accurate Riva Rocci s cuff (1899) was only 4 5 cm wide and gave falsely high readings as shown by von Recklinghausen (1901) who introduced the standard 5 inch cuff (12 7 cm) During the last twenty years it has been pointed out repeatedly that this cuff was designed for an adult with an average sized arm when applied to a large arm or thigh the

reading obtained is too high, and when applied to a small arm the reading is too low (Ragan and Bordley 1941) For infants the cuff should not exceed 2 5 cm (Woodbury Robinow and Hamilton 1938) for young children it should be about 3 inches wide and for the outsized adult 7 or 8 inches wide Even with these precautions cuff readings only approximate those recorded directly by means of arterial puncture the systolic level averaging 8 mm Hg too low and the diastolic (taken at the point of muffling) 8 mm Hg too high (Bordley *et al* 1951) The point at which sounds cease altogether is actually nearer the true diastolic pressure and is gradually gaining favour on that account but it is technically a less satisfactory end point

AUSCULTATORY SILENT GAP—When there is hypertension sounds occasionally disappear as the cuff is inflated but reappear at higher levels In standing patients the gap is encouraged by allowing the arm to hang down and discouraged by elevating the arm (Berry 1940) Similarly the gap is favoured by inflating the cuff slowly and may be abolished by inflating it rapidly (Ragan and Bordley 1941) The phenomenon may be related to the development of a very high venous pressure distal to the cuff which causes the diastolic arterial pressure to rise well above its proper level thus diminishing the pulse pressure

IRREGULARITIES When there are ectopic beats the higher pressure of the beat that follows the ectopic should be ignored In auricular fibrillation only approximate readings can be obtained the systolic pressure should be taken at the point where the majority of beats come through the diastolic where the majority of beats become muffled As the blood pressure normally varies by a few mm Hg with respiration it may be suitably recorded to the nearest multiple of five

*Normal range*

THE NORMAL SYSTOLIC BLOOD PRESSURE lies between 95 and 150 mm Hg Whilst it is true that apparently normal subjects between the ages of 40 and 65 tend to have higher systolic pressures than those between 20 and 40 insurance companies well recognise the value of low figures and it is probable that the higher average pressures of the middle aged and elderly are due to atherosclerosis (Lewis 1938)

THE NORMAL DIASTOLIC BLOOD PRESSURE lies between 60 and 90 mm Hg The mean pressure approximates to the diastolic plus one third of the pulse pressure

Although these figures have been standard for a long time a det[illegible]ned attempt to raise the upper limits of normal has recently been [illegible]ade by Master Garfield and Walters (1952) In their well reasone[illegible] [illegible]ograph these authors have made a strong plea for accepting a figur[illegible] 100 plus the age of the patient in years plus 5 to 10 mm Hg as t[illegible] [illegible]per limit of normal systolic pressure for middle aged men (aged 40 [illegible]) and a figure 5 mm Hg higher for women between the ages of [illegible] They also

provided good evidence for raising the upper limit of the normal diastolic pressure from 95 to 100 mm Hg in men and women over 50 years of age

IN CHILDREN the blood pressure averages 90/60 between the ages of 3 and 9 95-100/60-65 between the ages of 10 and 12 and 105 65 between the ages of 13 and 15 (Judson and Nicholson 1914)

A COMMON SOURCE OF ERROR in blood pressure estimation results from failure to obtain a reasonably basal reading this may be due to impatience or to lack of recognition of emotional or other physiological factors Whenever the pressure is found to be raised the cuff should be left in position so that a second reading may be taken at the end of the examination Casual measurements in healthy young adults who are a little anxious often register 160/90 mm Hg but if the patient is put at ease and allowed to rest quietly on a couch this figure may fall steadily to normal levels It must be thoroughly understood that the maximum normal blood pressure of 150/90 mm Hg is meant to be at ease The question of pre hypertensive levels will be discussed later

Slight *disparity between readings taken from each arm* is common especially in atherosclerotic and hypertensive subjects but the difference rarely exceeds 5 mm Hg (Amsterdam and Amsterdam 1943) The blood pressure is sometimes taken in the legs with the cuff above the knee and the stethoscope in the popliteal fossa In the average normal individual in the horizontal position *the blood pressure in the legs* reads 20 to 40 mm Hg above that in the arms The discrepancy is due to using the standard cuff as previously described, and is not found when records are obtained by means of direct arterial puncture (Loman *et al* 1936) *In the standing position* the systolic pressure in the arms measured at heart level usually shows no appreciable change but in 33 per cent of normal subjects it drops about 10 to 15 mm Hg the diastolic pressure rises about 5 mm Hg in 48 per cent of normal subjects drops about 5 mm Hg in 12 per cent and remains unchanged in 40 per cent (Currens 1948) *At death* all intravascular pressures level out at 14 to 22 mm Hg This is known as the static pressure and may be reached during periods of prolonged asystole (Dowling *et al* 1952 Anderson 1954)

## THE OCULAR FUNDI

Before leaving the peripheral vascular system the ocular fundi should be examined The ophthalmoscope should be used with both eyes open and with either hand so that one may hold the instrument with the right hand when examining the patient s right eye and with the left hand when examining his left eye There are four features of particular interest to the cardiologist the appearances of the disc the state of the arteries the presence of hæmorrhages and the presence of exudates

PAPILLŒDEMA may occur in acute or chronic renal hypertension and necessarily in malignant hypertension (by definition) In these cases swelling of the disc is usually attributed to the high cerebro spinal

pressure that is commonly found but it is by no means clear just why the C S F pressure should be raised. Papillœdema may also occur in anoxic cor pulmonale (see frontispiece) and here again the C S F pressure is high possibly because of increased filtration through the choroid plexus resulting from cerebral vasodilatation due to carbon dioxide retention. Papillœdema is seen occasionally in bacterial endocarditis when it is usually associated with acute nephritis also in temporal arteritis and rarely in periarteritis nodosa. When found in association with other kinds of cardiovascular disease cerebral tumour is more likely to be responsible. It does not occur in congestive heart failure or in chronic constrictive pericarditis nor even in the majority of cases of superior vena cava obstruction despite jugular venous pressures up to 30 mm Hg and correspondingly high C S F pressures.

THE CALIBRE OF THE RETINAL ARTERIES should be compared with that of the veins and expressed as an A/V ratio the normal being 4 5 or 5/5. It should be understood that only the blood stream flowing through the artery or vein is seen the wall of the vessel itself being normally invisible. The lighter longitudinal band in the centre represents reflection of light from that part of the vessel which lies in a plane more or less at right angles to the beam from the ophthalmoscope. The state of the arteries in hypertension is described in Chapter XVI. Here it may be added that both arteries and veins become very small in cases of optic atrophy that a thrombosed artery is represented by a white streak that remarkably large veins may be physiological and that vasodilatation causes venous rather than arterial pulsation (this is well seen in cases of aortic incompetence).

HÆMORRHAGES Retinal hæmorrhages are discussed in relation to hypertension in Chapter XVI. They may also occur in bacterial endocarditis, diabetes mellitus acute nephritis periarteritis nodosa disseminated lupus temporal arteritis and any condition which may give rise to petechiæ. Extensive hæmorrhage may follow venous thrombosis. Sometimes its cause is not apparent.

EXUDATES Retinal exudates associated with hypertension are described in Chapter XVI. Exudate may also occur in any of the conditions specified in the preceding paragraph.

## JUGULAR VENOUS PRESSURE

### *General considerations*

The jugular venous pulse should be analysed clinically in terms of pressure and wave form it is hard to conceive of any physical sign that is more informative.

It should first be understood that the mean intravascular pressure generated by left ventricular systole and maintained by aortic valve closure gradually falls as energy is expended overcoming the peripheral resistance so that from a level of about 90 mm Hg in the aorta and major arteries

it falls to around 70 mm Hg in the smallest arteries 30 mm Hg in the smallest arterioles about 10 mm Hg in the venules and around zero in the great veins When there is arteriolar vasodilatation the venous pressure tends to rise a little and when there is arteriolar vasoconstriction it tends to fall If the venous return from any part is totally obstructed the pressure in the veins distal to the obstruction rises rapidly to arterial level provided the arteries are not also obstructed The central venous pressure is also influenced by right atrial contraction and relaxation closure of the tricuspid valve right ventricular diastolic tone and the intrathoracic pressure (normally negative)

As seen at the bedside the jugular venous pulse is the oscillating top of the distended proximal portion of the internal jugular veins and represents volumetric changes which faithfully reflect the right atrial pressure at all stages of the cardiac cycle Thus if the mean pressure in the right atrium is 10 cm of water the jugular veins will be distended to an average point in the neck exactly 10 cm vertically above the centre of the right atrium (disregarding the specific gravity of blood which is 1 056) The veins above this level are collapsed for the actual pressure within them is less than atmospheric This introduces another facet of the subject which it may be as well to clarify at once The pressure at any given point in the circulation is always expressed in relation to a fixed geographical reference point usually the heart itself In the simple illustration just mentioned the actual pressure at the top of the jugular venous pulse is zero but if the base line of the manometric system is set at heart level the reading becomes 10 cm of water which represents the *10 cm* height of water in the tube connecting the manometric base line to the needle in the vein Similarly the actual pressure in the inferior vena cava at a point 15 cm below heart level in the same illustration is 25 cm of water but the reading is still 10 in relation to heart level because the 15 cm column of water in the connecting tube exerts a negative pressure of 15 cm of water on the manometric system In this way the influence of gravity is removed from all pressure measurements a highly desirable condition because in a closed circuit such as the circulation the effects of gravity in the arterial and venous pressures are necessarily opposed and tend to cancel each other out in so much as the blood vessels do not behave like rigid tubes this annulment of the effects of gravity is far from perfect but natural adjustments normally compensate for the disparity

*Recognition of venous pulsation*

Venous pulsation in the neck can be recognised and distinguished from arterial pulsation in the following ways

1 The movement is soft diffuse and undulant
2 The pulse that is seen cannot usually be felt
3 With normal rate and rhythm there are two crests and two troughs per cardiac cycle

4 When timed against the carotid pulse only the first trough appears to coincide with systole This is the $x$ descent which follows the presystolic $a$ wave The second crest $v$ appears to be late systolic or early diastolic and the second trough $y$ is obviously diastolic (fig 2 14)

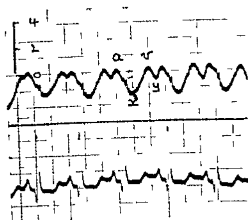



Fig 2 14—Normal central venous pulse recorded simultaneously with the electrocardiogram The $x$ descent is interrupted by a small $c$ wave or by a first heart sound artefact The rate of 116 beats per minute is too fast for the full development of $y$

5 The top level of pulsation normally drops to a lower level on inspiration and rises to a higher level on expiration passively following the changes in intrathoracic pressure

6 The jugular venous pressure usually rises on abdominal compression This may increase the intrathoracic pressure or raise the total intra abdominal venous pressure and it matters little to what part of the abdomen pressure is applied (fig 2 15)

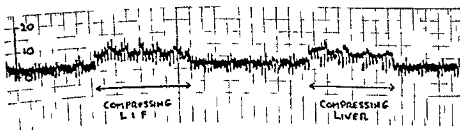



Fig 2 15—Rise of venous pressure on abdominal compression compressing the left iliac fossa is as effective as compressing the liver (Time marking 1 mm per sec)

The jugular venous pressure varies with posture being higher in the horizontal position and lower in the vertical owing to the influence of gravity

Cervical venous pulsation ceases if the jugular veins are compressed at the root of the neck

Light pressure of the finger against the root of the external jugular vein distends the upper part of the vessel On removing the finger the vein collapses to the level of the mean jugular venous pressure

*Clinical measurement of jugular venous pressure*

The most satisfactory reference point from which to measure the jugular venous pressure is the sternal angle Lewis chose this point because its relation to the right atrium is more or less stable being about 5 cm above the centre of the right atrium in both the horizontal and vertical positions The patient should be propped up at 30 60 or 90 degrees whichever position reveals maximum venous pulsation The vertical distance between the top of the oscillating venous column and the sternal angle represents the central venous pressure and is recorded in centimetres (of blood) above the sternal angle The incline of the patient when the measurement was made should also be recorded because the venous pressure varies with posture as previously stated (this has nothing to do with the relationship of the sternal angle to the right atrium)

The *normal jugular venous pressure* ranges between plus 3 cm and about minus 7 cm with reference to the sternal angle with the patient horizontal The mean right atrial pressure averaged minus 1 5 mm Hg with reference to the sternal angle in 50 normal controls studied by the author

*Causes of an elevated venous pressure*

The venous pressure may rise under a variety of physiological and pathological conditions in addition to heart failure

1 *Physical effort* raises the venous pressure owing partly to the squeezing action of skeletal muscular contraction on the veins and partly to peripheral vasodilatation the effect may be masked by reduction of the mean intrathoracic pressure resulting from hyperventilation The venous pressure rises sharply during a rigor

2 *Hyperkinetic circulatory states* due to heat fever pregnancy anæmia arterio venous aneurysm beri beri thyrotoxicosis Paget s disease of bone hypoxia or advanced disease of the liver are all associated with a rise of venous pressure which may be partly attributed to vasodilatation The cardiac output is raised and it may be difficult to be sure whether the heart is overloaded or not Amyl nitrite acetyl beta methylcholine and other vasodilators in therapeutic doses may have a similar effect

3 *An increased blood volume* is usually due to sodium retention and occurs physiologically in women during the pre menstrual phase and in

pregnancy it occurs pathologically in acute nephritis without denoting heart failure and can be induced artificially by feeding with salt and desoxycorticosterone acetate by pitressin A C T H therapy and of course by large intravenous infusions

4 *A sufficiently slow heart rate* whether due to heart block or not is usually associated with a rise of venous pressure owing to right ventricular resistance to overfilling To maintain an adequate cardiac output per minute the stroke output may have to be doubled Thus a rise of venous pressure does not necessarily mean congestive failure in cases of complete heart block

5 *An increased intrathoracic pressure* raises the jugular venous pressure but not the right ventricular filling pressure The effect is produced momentarily during the act of coughing and artificially by means of the Valsalva manœuvre Pleural effusion may have a similar effect and may be wrongly attributed to heart failure in consequence

6 *An increased intra abdominal pressure* probably acts indirectly by raising the intrathoracic pressure Tight corsets abdominal binders trousers too tight round the waist, obesity alone ascites pregnancy or even gross flatulence may each have this effect To witness alleged heart failure immediately relieved by undoing the top trouser buttons can be both embarrassing and instructive

7 *A raised intrapericardial pressure* from effusion increases the filling resistance of the right ventricle and so raises the jugular venous pressure Chronic constrictive pericarditis has the same effect

8 *Partial obstruction of the superior vena cava* raises the jugular venous pressure without abolishing pulsation only when the block is complete or very nearly so does venous pulsation cease *Obstruction of the inferior vena cava* may raise the jugular venous pressure indirectly by interfering with renal function and sodium excretion

9 *In tricuspid stenosis* the raised venous pressure is associated with a normal right ventricular diastolic pressure

10 *Space filling lesions affecting the right side of the heart* prevent proper filling of the right ventricle and include massive thrombosis of the right atrium tumour, constrictive endocarditis aneurysm of the interventricular septum and Bernheim s syndrome

11 *Giant* a *waves cannon waves* and *tricuspid incompetence* raise the jugular venous pressure during a particular phase of the cardiac cycle and will be considered in relation to the venous pulse (*vide infra*)

12 *Congestive heart failure* itself of course is the most important cause of an elevated venous pressure and is discussed in detail in Chapter VII hydræmia from sodium retention resistance to right ventricular over-

filling and sometimes functional tricuspid incompetence are all implicated

In all the pathological conditions mentioned above (apart from coughing and the Valsalva manœuvre) venous pulsation is preserved and with the exception of partial S V C obstruction the jugular venous pressure represents the right atrial pressure When the cervical veins are distended but do not pulsate, they are either obstructed at the root of the neck or there is total obstruction of the superior vena cava Obstruction of one or more cervical veins at the root of the neck may be due to kinking or local compression from neighbouring structures and may disappear at once if the relationship between the head and neck and the shoulder girdle is altered

*Therapeutic methods of raising the central venous pressure* include the horizontal posture (more effective if the legs are raised) leg binders exerting a subarterial pressure on as large a surface as possible from the toes to the hips overalls that can be inflated to any desired pressure intravenous infusions and salt with desoxycorticosterone Selective chemical venoconstrictors have not yet been discovered Arteriolar vasodilators are usually contra indicated because the blood pressure is too low in these cases and there is already too much blood laked in the periphery moreover many such substances are also venodilators

*Venous pressure lowering agents* include the erect or semi erect posture (sitting or propped up with the legs hanging down) venous tourniquets applied to the thighs venesection dehydration by means of sodium depletion (low sodium diet kation exchange resins carbonic anhydrase inhibitors and mercurial diuretics) and chemical venodilators such as theophylline tetraethylammonium and hexamethonium

## THE JUGULAR VENOUS PULSE

Precise analysis of the cervical venous pulse and measurement of the height of each individual wave with reference to the sternal angle is not only possible at the bedside but highly desirable In the previous section on the jugular venous pressure there was a noticeable lack of precision concerning the wave responsible for the pressure actually measured this defect will now be remedied

*Definition of waves*

The jugular venous pulse consists essentially of four waves *a* *x* *v* and *y* (fig 2 16). The first and third waves (*a* and *v*) are crests the second and fourth (*x* and *y*) troughs A fifth wave known as *c* another crest, may interrupt the x descent and a final upward movement often quite sharp follows *y* There is some advantage in allotting the letter *z* to the point reached by this last movement before the inscription of the *a* wave of the next cardiac cycle

*The* a *wave* is due to right atrial systole and disappears in auricular fibrillation

*The* x *descent* is due chiefly to atrial relaxation and also disappears in

auricular fibrillation (fig 2 17) for this reason it is difficult to believe that withdrawal of the atrioventricular septum towards the cavity of the right ventricle a movement known as descent of the base is mainly responsible for x

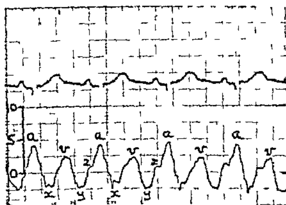



Fig 2 16—Normal right atrial pressure tracing c is represented by a small notch towards the end of the x descent the rise of pressure from the trough y to the zero point z before atrial contraction is well shown

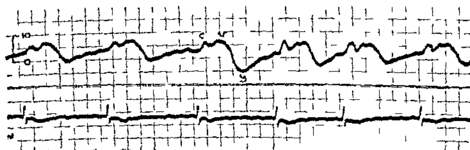



Fig 2 17—Pressure pulse from the right atrium in a case of mitral stenosis with auricular fibrillation showing absence of the x descent

*The c wave* which may interrupt the *x* descent was first attributed to tricuspid valve close (Potain 1867) and later to a carotid artefact (MacKenzie 1902) While admitting that a *c* wave due to mitral valve closure is usually prominent in direct left atrial pressure tracings in cases of mitral stenosis (fig 2 18) the writer has found relatively few conspicuous *c* waves due to tricuspid valve closure in well over a thousand right atrial pressure tracings obtained from a wide variety of cases including 50 normal subjects There is a great deal of difference between the forceful closure of the mitral valve in mitral stenosis and the gentle apposition of the tricuspid leaflets in normal hearts Clinically *c* is unobstrusive in the majority of

jugular venous pulses the trough x usually accompanying the early part of systole in cases with normal rhythm (figs 2 14 and 2 16) The c wave of external jugular phlebograms is always far more prominent (fig 2 19) and as shown by Mackenzie represents the carotid pulse itself

There is some evidence that well defined c waves due to tricuspid valve closure may occur in atrial septal defect and they might be expected in any condition in which the tricuspid valve is wide open at the moment the ventricle contracts

*The* v *wave* represents a rising right atrial pressure due to temporary obstruction of the blood flow during ventricular systole When there is

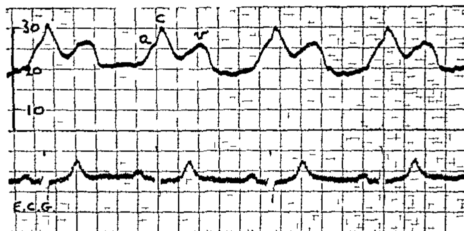



Fig 2 18—Left atrial pressure tracing showing a powerful c wave closely following a in a case of mitral stenosis

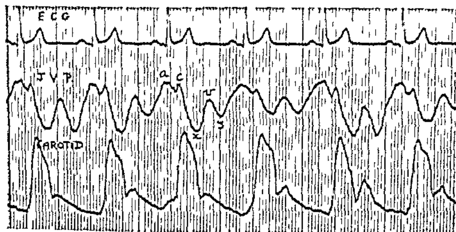



Fig 2 19—Conspicuous c wave in an external jugular phlebogram recorded simultaneously with the carotid pulse (see text)

normal rhythm it appears in late systole for it is at first overpowered by the x descent of atrial relaxation when there is auricular fibrillation however it starts with the first heart sound and occupies the whole of systole (fig 2 17)

*The* y *descent* begins as soon as the tricuspid valve opens i e at the end of the period of isometric ventricular relaxation This of course is the down slope of *v* just as the *x* descent is the down slope of *a* As the tricuspid valve opens there is a potential pressure gradient between the slightly raised right atrial pressure and the rapidly falling right ventricular pressure but they equalise rapidly and appear to fall together to the trough *y*

*Return of pressure to the point* z is gradual or rapid according to the ease with which the right ventricle dilates In normal hearts the ascent is gradual for there is little resistance to right ventricular filling

*Normal venous pulse*

The normal jugular venous pulse oscillates gently around a mean level a little below zero with reference to the sternal angle Typical figures for *a x v y* and *z* are 0 −4 0 −3 −1 mm Hg respectively *a* and *v* being about equal in amplitude, and the greatest excursion being the x descent Only with heart rates below 90 beats per minute is there time for full inscription of all five waves With heart rates between 90 and 110 the zero point is not defined *a* succeeding *y* immediately With rates higher than 110 there is no time for the proper development of *y* *a* succeeding *v* just as the *y* descent starts and at a rate of around 150 *v* and *a* are wholly superimposed These figures are only approximate for they vary considerably according to the length of the P R interval and the duration of ventricular systole

Clinically it is usually easy to measure the height of *a* and *v* in centimetres above the sternal angle and *z* is not difficult with slow rates but the troughs *x* and *y* may have to be estimated only approximately In clinical notes the form of the venous pulse should be drawn and a figure representing the approximate pressure of each wave should be inscribed in the appropriate place

*Abnormalities of the jugular venous pulse*

*A giant a wave* (fig 2 20) measuring between 6 and 15 mm Hg above *v* is characteristic of severe pulmonary hypertension severe pulmonary stenosis tricuspid stenosis or tricuspid atresia (provided there is no free right to left shunt in any of them) It is presystolic abrupt and collapsing in quality (venous Corrigan) palpable transmitted to the liver and usually associated with right atrial gallop and a conspicuous P pulmonale It alters little if at all with change of posture and increases in amplitude both with inspiration (fig 2 21) and abdominal compression The powerful right atrial contraction responsible for the giant *a* wave seems to be due to increased resistance to right ventricular filling over a long period of time

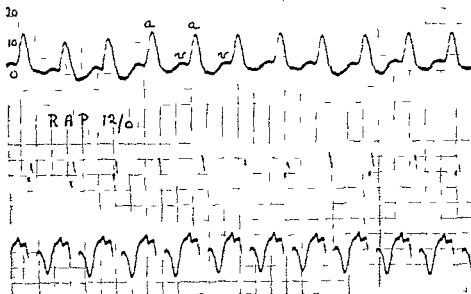



Fig 2 20—Giant *a* wave in pulmonary valve stenosis with reversed interatrial shunt

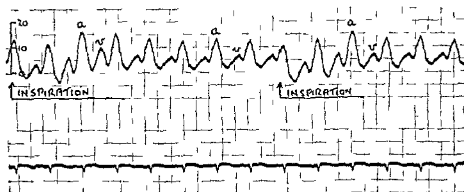



Fig 2 21—The effect of respiration on the giant *a* wave

It does not occur in ordinary cases of heart failure in which the right ventricular diastolic pressure is raised and it is usually absent in both Eisenmenger s complex and Fallot s tetralogy Teleologically in pulmonary hypertension and pulmonary stenosis it serves to increase the contractile force of the right ventricle in accordance with Starling s law which states that within certain limits the force of cardiac contraction is a function of fibre length When nodal rhythm has occurred fortuitously during cardiac catheterisation in several of these cases the right ventricular systolic pressure has fallen abruptly by 20 to 30 mm Hg (fig 2 22)

*A prolonged* a c *interval* occurs in partial heart block Clinically the interval between *a* and the carotid pulse can be graded easily enough into

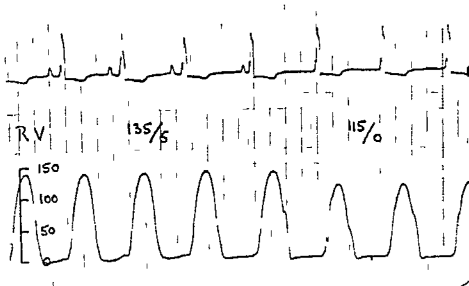



Fig 2 22—Right ventricular pressure tracing from a case of severe pulmonary valve stenosis showing a sudden fall in pressure of at least 20 mm Hg with the onset of nodal rhythm (see text)

short (P R interval around 0 12 sec ) average (P R 0 16 sec ) rather long (P-R 0 20 sec ) and obviously prolonged (P R 0 24 sec ) When P R is longer than 0 24 second *a* tends to fuse with *v* as it does with sinus tachycardia and normal conduction

*Independent* a *waves* occur in complete heart block They are usually of small amplitude and likely to be overlooked unless the venous pulse is studied very carefully

*Cannon waves* are more obvious and occur whenever the right atrium contracts against a closed tricuspid valve i e when the P wave of the electrocardiogram falls between the end of QRS and the end of T This occurs irregularly in complete heart block (fig 2 23) and with multiple ectopic beats and regularly with nodal rhythm paroxysmal nodal tachycardia and partial heart block with an extremely long P R interval

A cannon wave is *not* a summation effect but a particular form of giant *a* The whole of the energy released by right atrial contraction is translated into pressure because forward flow is impossible The word is used in the sense of rebound apt enough since the tricuspid valve is shut in the face of the oncoming wave from the atrium

In complete heart block cannon waves are *not* synchronous with cannon sounds on the contrary the first heart sound associated with a cannon wave is relatively quiet The cannon sound in heart block refers to the explosive first sound that is heard when the atria contract about 0 10 second before the ventricles so that the mitral cusps flung wide open by atrial contraction are slammed shut by the quickly succeeding ventricular systole —another kind of rebound altogether if the word is still used in that sense

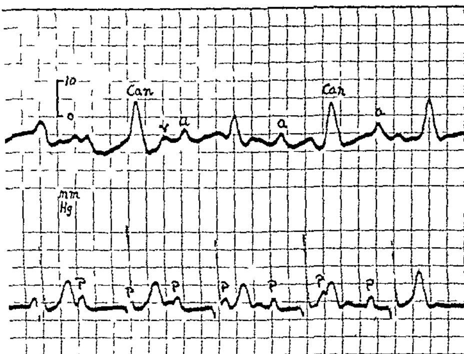



Fig 2 23—Irregular cannon waves in the central venous pulse in a case of complete heart block cannons are seen whenever P falls between Q and the peak of T in the electro cardiogram

In 2 1 heart block alternate *a* waves usually broaden *z* and are incon spicuous but if they fall a little earlier regular cannon waves may be observed

Ectopic beats may cause cannon waves in several different ways An atrial ectopic may coincide with the previous ventricular systole Nodal ectopics usually cause the atria and ventricles to beat together as in nodal rhythm Ventricular ectopics cause cannon waves when they are only slightly premature so that they coincide with normal atrial contraction excited by discharge of the sinus node

Paroxysmal tachycardia need not necessarily be nodal to cause cannon waves Atrial tachycardia may do so when there is 2 1 fatigue block (if atrial contraction is forceful enough) or when P R is prolonged so that P falls before the end of the preceding T wave and ventricular tachycardia may cause irregular cannon waves when atrial contraction is independent

*Absence of a conspicuous x descent* is invariable in auricular fibrillation instead there is a broad positive systolic wave *z* sometimes initiated by a small *c* wave (fig 2 17) If the *x* descent were due chiefly to downward movement of the atrial floor during ventricular systole it should be influenced but little by auricular fibrillation

The *x* descent is diminished in tricuspid incompetence but may still be recognised when the rhythm is normal (fig 2 24) The *x* descent is similarly

absent from direct and indirect left atrial pressure pulses in cases of auricular fibrillation but may be present in mitral incompetence when the rhythm is normal

*Large v waves* are especially characteristic of tricuspid incompetence with auricular fibrillation (fig 2 25) and are transmitted to the liver The

Fig 2 24—Case of tricuspid valve disease (due to lupus) with stenosis and incompetence and *with normal rhythm* showing an $x$ descent before the v wave The bottom tracing is a *continuous* record of the pressures obtained as the catheter was withdrawn from the pulmonary artery (left) to the right atrium (right) note the pressure gradient across the tricuspid valve




Fig 2 25—Case of tricuspid incompetence with auricular fibrillation showing a large v wave

high amplitude of the systolic wave is augmented by the deep y trough which follows

*A deep y descent* or diastolic collapse of the venous pulse was first described in relation to chronic constrictive pericarditis (Friedreich 1864) In these cases the venous pressure is high throughout the cardiac cycle except for a short period immediately following the opening of the tricuspid valve when blood from the right atrium pours into the relaxing right ventricle Right atrial and ventricular pressures equalise rapidly and the small cavity of the right ventricle is quickly filled further filling is resisted by the rigid pericardium so the pressure rises again sharply during the rest of diastole (fig 2 26)

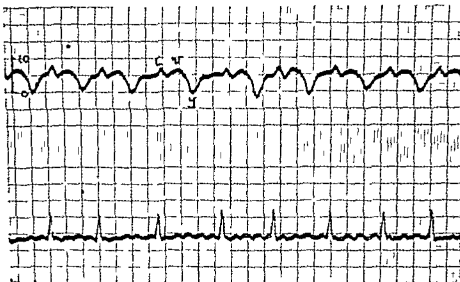



Fig 2 26—The steep y descent in a case of Pick s disease

It was at first thought that the rigid pericardium tensed inwards during systole (either alone or in conjunction with the chest wall) recoiled like a spring in early diastole and so created a powerful negative pressure which explained the diastolic venous collapse *but although such a mechanism* may exist it is superfluous to the thesis for the same phenomenon occurs in any condition in which the venous pressure is very high provided there is no obstruction at the tricuspid valve (fig 2 27) In severe right ventricular failure for example the same high potential pressure gradient between atrium and ventricle must exist immediately the tricuspid valve opens ventricular filling and equalisation of pressures are just as rapid and further filling is resisted by the already overstretched fibres of the failing myocardium the stroke output in these cases is just as small as in Pick s disease

Fig 2 27—Jugular phlebogram showing a steep y descent and deep y trough in a case of mitral stenosis with extreme pulmonary hypertension

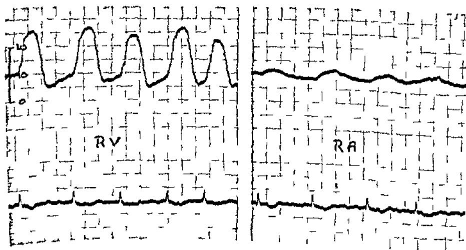



Fig 2 28—Case of tricuspid stenosis showing a slow y descent

*A slow y descent* following *v* despite a high venous pressure is characteristic of tricuspid stenosis (fig 2 28), for rapid equalisation of jugular and right ventricular pressures is then impossible The same sluggish *y* descent is seen in left atrial pressure tracings in cases of mitral stenosis (Owen and Wood 1955) Again in tricuspid stenosis there is no rapid rise of pressure following the *y* trough as there is in heart failure and Pick's disease so that *z* is little if at all higher than *y*

## OTHER CLASSICAL SIGNS OF HEART FAILURE

If the jugular venous pressure is raised in a manner suggesting heart failure a *distended and often tender liver* can usually be palpated If the liver edge cannot be felt the epigastrium and right hypochondrium should be percussed a good resonant note up to the right costal margin anteriorly excludes significant enlargement A high venous pressure without hepatic enlargement suggests obstruction of the superior vena cava enlargement of the liver without a rise of venous pressure should never be attributed to heart failure

*Œdema* does not necessarily accompany a raised venous pressure due to heart failure as explained in Chapter I on the other hand cardiac œdema does not occur without a raised venous pressure The swelling is maximal round the ankles in ambulant patients but may be chiefly sacral in those confined to bed Its mechanism is discussed in Chapters I and VII

*Physical signs of pulmonary venous congestion* due to left ventricular failure are usually wanting Basal rales are notoriously unreliable being absent in the majority of cases and often having another interpretation when present In acute pulmonary œdema however fine crepitations can be heard over a wide area of both lungs The explanation for these two statements is simple enough a rise of pulmonary venous pressure up to 30 mg Hg causes no exudation of serum into the alveoli and therefore does not give rise to crepitations only when the pulmonary venous pressure exceeds the osmotic pressure of the plasma does such exudation occur i e in acute pulmonary œdema When basal rales are heard in either left ventricular failure or mitral stenosis in the absence of pulmonary œdema increased bronchial secretions are culpable but although pulmonary venous congestion may be responsible for the increased bronchial activity the sign is so common in simple bronchitis or bronchiolitis that it cannot be accepted as reliable evidence of heart failure

## EXAMINATION OF THE HEART

Having gleaned as much information as
from examining the peripheral vascular s,
from searching for signs of failure one may
heart itself and duly inspect palpate pe

*Inspection*

The position and character of the cardiac impulse if visible and of any other thoracic pulsation should be noted In this way left or right ventricular hypertrophy, gallop rhythm dilatation of the pulmonary artery and aortic aneurysm may be detected Præcordial deformity may be observed and if due to the heart indicates its enlargement during the period of thoracic growth Depression of the sternum or other thoracic deformity should be noted for it may alter the shape or position of the heart Systolic indrawing of the thoracic wall is not abnormal if it occurs over the right ventricle and is exaggerated in this situation when the left ventricle is alone enlarged and it may be seen in the anterior axillary line or beyond when there is gross enlargement of the right ventricle As a sign of adherent pericardium it should be looked for posteriorly over the last two ribs as described by Broadbent (1895)

*Palpation*

The apex beat which is a geographical point should be determined by locating the exact site of the left ventricular impulse The physician s hand should be placed over the region of the fifth left intercostal space in the nipple line in order to ascertain its approximate position the middle finger should then be directed vertically over it and shifted about until the maximum thrust is located This, rather than the lowest left point of such pulsation, is the apex beat Its position should be recorded with reference to the intercostal spaces to the mid line and to the mid clavicular line If it is located beyond these confines the possibility of displacement from scoliosis elevation of the diaphragm or from pulmonary or pleural lesions should be considered before concluding that the heart is enlarged

The character of the cardiac impulse is as important if not more important than its position (the apex beat) it should be sensed both with the palm of the hand and with the finger tip A steady heaving impulse means left ventricular hypertrophy and is felt in aortic stenosis and systemic hypertension A hyperdynamic impulse is also forceful but has greater amplitude and is more abrupt and lively it signifies an overfilled ventricle usually working against a low resistance as in aortic incompetence mitral incompetence patent ductus ventricular septal defect and the hyperkinetic circulatory states Both heaving and hyperdynamic left ventricular impulses are usually associated with increased retraction of the chest wall overlying the right ventricle slight retraction in this region being normal A steady heave over the right ventricle about the left parasternal line is felt in pulmonary hypertension and pulmonary stenosis A hyperdynamic right ventricular lift is more tumultuous and is characteristic of the overfilled right ventricle of atrial septal defect A strong impulse over the right ventricle is usually associated with conspicuous retraction further to the left where the apex beat (left ventricular impulse) might have been expected This rocking movement is very easily seen and is the reverse

of the left ventricular rock described above When the left ventricle is small or rotated posteriorly and the right ventricle unimpressive no cardiac impulse may be felt at all only the tap of the first heart sound being appreciated this is typical of uncomplicated mitral stenosis when the first heart sound is accentuated

Palpation of the heart sounds in general can hardly be avoided not only the first but also systolic ejection clicks both elements of the second sound the opening snap of mitral stenosis the third sound and any kind of gallop are all frequently palpable when present

Palpation may next be used to detect the presence of thrills preferably in forced expiratory apnœa This manœuvre brings the heart and great vessels closer to the chest wall encourages the lung to retract from its buffering position and lessens the chance of confusing cardiac with respiratory phenomena Tricuspid thrills alone are better appreciated during inspiration The vibration sense of normal individuals varies considerably, but increased perception comes with experience and good technique

Practically all important murmurs, including certain functional murmurs may be accompanied by a thrill Indeed, of the twenty one different types of murmur described later in this chapter only the Carey Coombs murmur of active rheumatic carditis and the cardio respiratory murmur are never so accompanied

*Percussion*

The value of percussing the heart has given rise to much dispute many modern cardiologists maintaining that its place has been taken by the far more accurate and fertile method of radiography The older school however modestly suggest that it is a useful bedside method which gives reliable and helpful information if practised diligently and if its limitations are appreciated Certainly if a fluoroscope is available percussion is pointless but a fluoroscope may not be available or the patient may be so ill that only a portable X ray machine can be used and the distorted skiagram so obtained is liable to gross misinterpretation In such cases percussion may be of value and by constant practice the physician should learn what can and what cannot be expected from it

The approximate position of the left border of the heart may be checked when the apex beat is difficult to locate and dullness beyond the known or probable confines of the apex beat may sometimes be detected in cases of pericardial effusion

It is impossible to determine the right border of the heart by percussion unless there is aneurysmal dilatation of the right atrium On the other hand pericardial effusion even of moderate degree can often be demonstrated

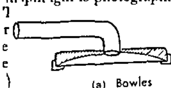
It was once customary to speak of relative and absolute cardiac dullness the latter being the note heard over the area of heart not covered by lung

but it is doubtful whether this distinction can be maintained Diminution or absence of cardiac dullness however is a useful sign of emphysema

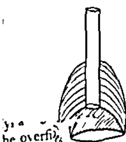
Percussion at the base may be rewarded in pericardial effusion, there being characteristic dullness in the second left interchondral space when the patient lies flat also in substernal goitre and in anterior aneurysm of the aorta when a band of dullness extends laterally from the manubrium sterni

## AUSCULTATION

When a man buys a tool for some specific purpose he usually takes care that it is the best available for the particular job in hand It is therefore strange that a superstition has grown up within the medical world that the older and more disreputable a stethoscope the better that it is not the stethoscope which matters but the man behind it This of course is nonsense When a student fails to hear a murmur which is heard easily by another exchange of stethoscopes quickly leads to mutual understanding There is another curious tradition fostered by many who appreciate the value of a good stethoscope that the chest piece must be bell shaped and that any other type especially the flat diaphragm (Bowles) is pernicious This doctrine is as unreasonable as the first for there is no doubt that certain high pitched sounds especially aortic diastolic murmurs and faint tubular breathing which can be heard with ease through a Bowles may be inaudible through a bell The physical laws which govern auscultation have been studied by Rappaport and Sprague (1941 and 1951) The diameter of the Bowles chest piece should be about 1½ inches the cup should be shallow and its edge sharp (fig 2 29a) Good material for the diaphragm is photographic or X ray film washed clean in hot water, and cut to shape The rubber tubing should be thick about 10 inches long and should fit snugly to the connections The internal calibre of the whole system including the metal binaurals and the hole in the centre of the chest piece should be one eighth of an inch A good bell stethoscope (fig 2 29 b) is better for detecting low pitched sounds such as soft mitral diastolic murmurs moreover its range of sensitivity may be increased by varying the force with which it is applied to the chest wall Light contact accentuates low pitched sounds firm pressure high pitched sounds The cup should not be too deep and its diameter not less than one inch



(a) Bowles



(b) Bell

2 29—Binaural stethoscopes

There are two other types of stethoscope which deserve comment the monaural wooden instrument of by gone days and

the differential stethoscope (symballophone) The rigid wooden stethoscope is rarely used nowadays but by combining aural and tactile senses it facilitates the recognition of gallop rhythm The differential stethoscope is constructed as shown in figure 2 30 and may be used to compare the timing of sounds originating at different sites and to determine the *direction in which a murmur is propagated* (Kerr *et al* 1937)

Auscultation of the heart can only be learned at the bedside but the following advice may be helpful to students The præcordium should be examined all over not just at areas where individual valve sounds are expected gallop rhythm pericardial friction and certain important murmurs will not then escape notice It is enough to listen to one thing at a time thus when an expert hears a soft elusive mitral diastolic murmur hitherto overlooked it is not necessarily because he has better ears or a better stethoscope, but because he has acquired a more selective power of concentration Basal murmurs and pericardial friction are heard most easily in expiratory apnœa tricuspid murmurs during inspiration mitral murmurs in the left lateral position especially when the heart slows down after exercise Heart sounds should be timed against carotid pulsation if difficulty is experienced due to tachycardia the heart may be slowed by carotid sinus compression

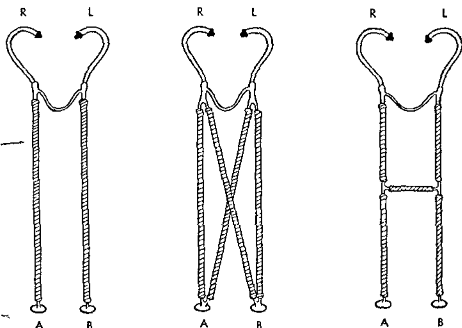



Fig 2 30—The differential stethoscope (3 varieties) Sounds travelling from A to B reach the right ear before the left giving the impression of movement in that direction

(Leatham and Vogelpoel 1954) they are also best heard in the third left space at the sternal edge but are not transmitted to the apex beat

If the definition of the first heart sound is extended to include vascular vibrations occurring at the end of the isometric contraction phase (Braun Menendez 1938) then an ejection click may be regarded as the second component of a widely split first sound There is an obvious advantage, however, in using the term aortic or pulmonary ejection click to describe this vascular sound and restricting the term split first sound to mean separation of mitral and tricuspid components only

*The second heart sound* is due to aortic and pulmonary valve closure The aortic element is heard best in the aortic area in the neck and at the apex beat and the pulmonary element in the pulmonary area In normal individuals both elements can usually be heard in the second and third left interchondral spaces close to the sternal border In children and adolescents the split is often obvious (grade II) particularly towards the end of inspiration The first element is aortic, the second pulmonary The lag of P2 during inspiration has been attributed to prolongation of right ventricular systole from increased filling (Leatham 1954) In atrial septal defect the split fails to widen on inspiration

*Pathological splitting* (grade III) is due to delay in pulmonary valve closure and is usually due to right bundle branch block delay in the emptying time of an overfilled right ventricle, or pulmonary stenosis In these cases the split may approach 0 1 second in width (grade I=0 02–0 03 sec grade II=0 04–0 05 sec) Slight delay in aortic valve closure may bring the two elements together and so cause a single second heart sound In aortic stenosis and left bundle branch block the aortic element may lag behind the pulmonary element a reversed split so caused tends to close on inspiration and widen on expiration and can thus be recognised by its paradoxical behaviour (Leatham 1954)

Recognition of a split second heart sound at once proves that both semilunar valves are functioning and thus excludes persistent truncus arteriosus pulmonary atresia and severe pulmonary stenosis although a very faint and delayed P2 can sometimes be heard in the last When the split is wide the intensity of the pulmonary element helps to distinguish pulmonary stenosis (P quiet) from right bundle branch block or atrial septal defect (P normal or rather loud) [4]

*Accentuation of the second heart sound* may result from systemic or pulmonary hypertension the clinical circumstances and the site of maximal intensity may decide which but sometimes it is only possible to be sure if there is sufficient splitting If the ascending aorta or pulmonary artery is unusually close to the anterior surface of the chest either because it is abnormal or because it is scantily covered by lung and chest wall the second heart sound is also loud Conversely *a soft or absent second heart sound* is usual in emphysema

About midway between the second and third heart sounds or about

0 08-0 1 second after A may be heard the *opening snap of mitral stenosis* (fig 2 31e) the sharp extra sound is due to the abrupt flapping back of the mitral cusps at the end of the period of isometric relaxation i e when the rapidly falling left ventricular pressure drops below the raised left atrial pressure The opening snap is best heard in expiration at the lower left sternal edge over the root of the aorta and over the left ventricle at the apex beat It is discussed more fully in relation to mitral valve disease in Chapter X

*The physiological third heart sound* (fig 2 31f) was well described by Gibson (1907) It is soft low pitched and often accompanied by a palpable shock it is more or less localised to the apex beat varies in intensity with respiration and is accentuated when the subject lies on the left side It may be heard in the great majority of children in about 50 per cent of young adults, occasionally in the middle aged and rarely in the elderly Phonocardiography shows that the third sound coincides with the latter half of the descending limb of the *v* wave of the jugular phlebogram i e with the end of the period of rapid ventricular filling (Ohm 1913) it is attributed to sudden distension of the left ventricle at this time (about 0 15 sec after the onset of A )

The third heart sound is accentuated by any condition which encourages rapid left ventricular filling e g mitral incompetence ventricular septal defect patent ductus Pick s disease the hyperkinetic circulatory states and left ventricular failure In the last of these examples the triple rhythm produced by the development of the third heart sound is called diastolic gallop and will be discussed more fully in Chapter VII

## *MURMURS*

There are at least twenty different heart murmurs which can be recognised by means of simple auscultation

1 *The apical presystolic murmur of mitral stenosis* (fig 2 32a) This is a left atrial systolic murmur left atrial contraction increasing the blood flow through the narrow mitral orifice towards the end of diastole It sounds crescendo especially when it suddenly augments a fading diastolic rumble and ends abruptly with an accentuated first heart sound but is not necessarily so The murmur is best heard with the bell stethoscope when the patient lies on the left side and is often accompanied by a thrill

2 *The presystolic murmur of Austin Flint* (1862 1886) may be heard in any form of well developed aortic incompetence and is generally believed to be due to vibrations of the anterior (aortic) cusp of the mitral valve which is agitated by the opposing forces of aortic reflux and left atrial contraction (Da Costa 1908) It is indistinguishable in quality and timing from the presystolic murmur of mitral stenosis Phonocardiograms have confirmed the reality of the murmur in cases which have been proved later to have normal mitral valves at necropsy (Currens *et al* 1953)

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2 *The presystolic murmur of Austin Flint* (1862 1886) may be heard in any form of well developed aortic incompetence and is generally believed to be due to vibrations of the anterior (aortic) cusp of the mitral valve which is agitated by the opposing forces of aortic reflux and left atrial contraction (Da Costa 1908) It is indistinguishable in quality and timing from the presystolic murmur of mitral stenosis Phonocardiograms have confirmed the reality of the murmur in cases which have been prov[illegible] to have normal mitral valves at necropsy (Currens *et*

3 *The presystolic murmur of tricuspid stenosis* is similar in quality timing and mechanism to its mitral counterpart but is heard at the tricuspid area instead of at the apex beat and is appreciably louder during inspiration

4 *The apical pansystolic murmur of mitral incompetence* (fig 2 32b) This begins early immediately after the first heart sound as soon as the pressure

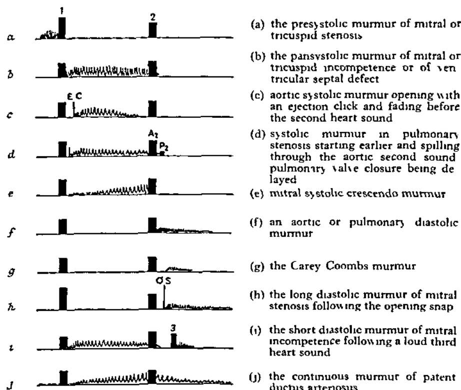



Fig 2 3 —The chief murmurs

in the left ventricle rises above that in the left atrium It also ends late embracing the aortic element of the second sound for the left ventricular pressure is still well above that in the left atrium when the aortic valve closes A thrill is common in organic cases but rare when the leak is functional

5 *The pansystolic murmur of tricuspid incompetence* is similar to its mitral counterpart except that it is heard best in the tricuspid area and is much louder during inspiration

6 *The pansystolic murmur of ventricular septal defect* (Roger 1879) is very like the murmur of mitral (or tricuspid) incompetence in quality and timing for the ordinary relationship between left and right ventricular pressure is not very greatly different from the relationship between left ventricular and left atrial pressure The murmur is heard best however

in the third and fourth intercostal spaces at the left sternal edge and is not accentuated by inspiration A thrill can be felt in 90 per cent of cases

7 *The aortic systolic murmur* (fig 2 32c) This is heard over the carotids in the aortic area in the third left intercostal space at the sternal edge and at the apex beat It does not begin with the first heart sound proper but after a short interval when the aortic valve opens an interval which becomes obvious enough when an aortic ejection click signals the opening of the valve The murmur is also relatively short ending just before aortic valve closure Turbulence may be due to increased flow as in the hyper kinetic circulatory states to dilatation of the ascending aorta or to aortic valve disease—especially stenosis An aortic systolic thrill usually means stenosis but may occur exceptionally with the other conditions mentioned

8 *The pulmonary systolic murmur* (fig 2 32d) This is more or less con fined to the pulmonary area and third left intercostal space at the sternal edge but may be much lower when the turbulence is infundibular It also begins a little while after the first heart sound proper its onset coinciding with the pulmonary ejection click when that is present i e with the opening of the pulmonary valve at the end of the period of isometric contraction It usually lasts longer than the aortic systolic murmur, for the pulmonary valve shuts later than the aortic Turbulence may be due to increased flow as in atrial septal defect to dilatation of the pulmonary artery or to pul monary or infundibular stenosis A thrill is nearly always present when there is stenosis but is by no means rare in uncomplicated A S D

9 *The crescendo mitral systolic murmur* (fig 2 32e) To the human ear this seems to begin rather late in systole and waxes greatly to end abruptly with the second heart sound just when it has reached its maximum It is usually due to trivial mitral incompetence although some authorities have stated it is commonly innocent (Evans 1948) Just how its curious crescendo quality is produced is unknown

10 *The late basal or posterior systolic murmur of coarctation of the aorta* is attributed to turbulence set up at the stricture itself rather than in col lateral vessels The murmur sounds a little late and may spill through the second sound into early diastole It is heard in the epigastrium or over the lumbar spine when the stricture is in the abdominal aorta

11 *The diastolic murmur of aortic incompetence* (fig 2 32f) is relatively high pitched and best heard with the diaphragm type of chest piece It is situated in the aortic area down the left border of the sternum, and over the left ventricle at the apex beat The murmur begins immediately after the aortic second sound and when loud persists throughout diastole in diminuendo fashion When the leak is very slight, however the murmur may be faint and short and then its greatest intensity is appreciably after the second heart sound indeed when only maximum vibrations

heard the murmur appears to be separated from the second heart sound by a distinct gap This is because the greatest backward flow does not occur until the left ventricular pressure has fallen to zero A diastolic aortic thrill favours syphilis or a perforated cusp but not exclusively A whining diastolic murmur has a similar meaning

12 *The diastolic murmur of pulmonary incompetence* is similar in quality and timing to the aortic diastolic murmur but is usually confined to the second and third left intercostal spaces It is nearly always functional being due to pulmonary hypertension as described by Graham Steell (1888) or to dilatation of the pulmonary artery without hypertension occasionally it is due to organic disease of the valve as in pulmonary stenosis after bacterial endocarditis or valvotomy It may be accompanied by a thrill

13 *The soft apical diastolic murmur of active mitral valvulitis* was well described by Carey Coombs (1924) It is low pitched relatively short diminuendo and separated from the second heart sound by an appreciable gap representing the time interval between aortic valve closure and rapid ventricular filling (fig 2 32g) The murmur is best heard with the bell stethoscope when the patient lies on the left side and is attributed to turbulence set up by inflammatory thickening of the mitral cusps It is one of the few murmurs practically never accompanied by a thrill

14 *The functional apical diastolic murmur* due to a torrential mitral blood flow is similar to the Carey Coombs murmur in all respects It may be heard in patent ductus ventricular septal defect complete heart block thyrotoxicosis and anæmia The mitral diastolic murmur sometimes associated with coarctation of the aorta and congenital aortic stenosis is not yet fully understood but is probably either rheumatic or due to some degree of fibroelastosis

15 *The apical diastolic murmur of mitral stenosis* is louder and usually rougher than those just described and is commonly preceded by the mitral opening snap (fig 2 32h) The murmur is long and in well developed uncomplicated cases continues to the next first heart sound A thrill is frequently associated In many cases of organic mitral incompetence a rough mitral diastolic murmur is also heard but it is short and follows a loud third heart sound instead of a snap (fig 2 32i)

16 *The diastolic murmur of atrial septal defect* gives rise to the same triple rhythm cadence as mitral diastolic murmurs for it is almost certainly due to a torrential tricuspid blood flow The murmur may be heard best at the apex beat where it may encourage a false diagnosis of Lutembacher s syndrome or near the left sternal edge sometimes as high as the third space, but may be maximum anywhere over the dilated right ventricle It is characteristically accentuated by inspiration which increases the tricuspid blood flow but not that through the atrial septal defect

17 *The continuous machinery murmur of patent ductus* (Gibson 1900) often accompanied by a thrill is more or less localised to the pulmonary area It waxes during systole and early diastole and wanes in late diastole (fig 2 32j) A similar murmur is heard in aorto pulmonary septal defect

18 *Continuous murmurs* waxing and waning in similar fashion are also heard on either or both sides of the chest usually high up anteriorly in cases of pulmonary atresia and are due to broncho pulmonary anastomatic (arterial) communications single or multiple

19 *The jugular venous hum* discussed at length by Potain in 1867, is also continuous and phasic in quality Although best heard over the jugular veins themselves it may be first detected when auscultating the aortic or pulmonary area It is loudest in the sitting or standing position is sharply accentuated during inspiration, and usually disappears when the subject lies flat The murmur is also abolished immediately if the jugular blood flow is temporarily halted by digital compression on the vein (usually the right) or by the Valsalva manœuvre

20 Other *continuous machinery murmurs* over the heart may be caused by perforation of an aortic sinus into the pulmonary artery right ventricle or atrium or by coronary arterio venous fistula and over any part of the chest by pulmonary arterio venous fistula

21 *So called functional murmurs* have led to great confusion In a sense all murmurs are an expression of function and in a very strict sense some very important valve murmurs are functional e g certain mitral diastolic murmurs and the Graham Steell murmur If the term is used at all it should mean either murmurs due to turbulence set up by increased blood flow alone the anatomy of the heart at the site of origin of the murmur being normal or murmurs due to functional changes in anatomy In the first group functional murmurs so defined include aortic and pulmonary systolic murmurs associated with hyperkinetic circulatory states the pulmonary systolic murmur of atrial septal defect the mitral diastolic murmur of patent ductus ventricular septal defect etc and the jugular venous hum and in the second group we have the Austin Flint murmur the systolic murmurs of functional mitral or tricuspid incompetence basal systolic murmurs associated with functional dilatation of the aorta or pulmonary artery and the Graham Steell murmur of functional pulmonary incompetence

To dismiss a murmur as functional is unpardonable A functional murmur is not insignificant and is certainly not meaningless nor does it refer exclusively to extracardiac murmurs although at least one of these is functional e g the cardio respiratory murmur This is attributed to systolic decompression of some segment of lung which is compressed by the expanding heart during diastole thus it is a vesicular murmur similar to the sound of inspiration It varies with posture and respiration

## EXAMINATION OF OTHER SYSTEMS

Thorough examination of all the other systems of the body should never be neglected in a presumed cardiological case not only as a matter of principle but also because important clues to cardiovascular diagnosis may lie outside that system Partly to emphasise this point a special section has already been devoted to examining the extremities Space forbids dealing with these other systems in a comprehensive manner and since to do so in a niggardly fashion would be valueless no purpose would be served by pursuing the subject further

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# ELECTROCARDIOGRAPHY

ELECTROCARDIOGRAPHY was discovered in relation to the frog's heart by Kolliker and Muller (1856) and was proved applicable to the study of the heart in man by Waller (1887) who used a capillary electrometer and an antero posterior chest lead It was elaborated by Einthoven (1903) inventor of the string galvanometer and author of the famous triangle which bears his name and used extensively by Lewis (1925) in his well known researches on abnormalities of rhythm In recent years many attempts have been made to place electrocardiography upon a more scientific and less empirical basis and considerable success has been achieved in this respect especially by Wilson and his colleagues (1930 *et seq*) It is not easy (or necessary) for the ordinary physician unless he also be a physicist and mathematician to grasp the electrical details involved but the following simplified account will be readily understood

Certain molecules in the resting cardiac muscle cell dissociate into positive and negative ions The positively charged ions (cations) are distributed on the outer surface the negatively charged ions (anions) within (Curtis and Cole 1941) Such a cell is in a state of electrical balance and is said to be polarised (fig 3 01a) When the cell is excited its polarity is reversed the negative charges coming to the surface the positive charges passing within and the cell is said to be depolarised (fig 3 01b) It should be clear that when a number of cells are clustered together all in the resting polarised state or all in the excited depolarised state there can be no potential differences anywhere on their collective surface If a group of cells were in the process of being excited however those already depolarised would possess negative surface charges whereas those still polarised would have positive surface charges and the collective surfaces of the two sets would yield a potential difference (fig 3 01c) This constitutes a doublet (Craib 1930) dipole (Ashman 1948) or double layer (Bayley 1943) Thus when an excitatory wave flows through cardiac muscle, its head is electrically positive and its tail negative (fig 3 01d) If electrodes are placed at A and B and connected to a galvanometer an electrical current flows from B to A through the galvanometer and from A to B through the tissue The excitatory process or accession wave as it is called causes a very rapid or almost instantaneous reversal of cellular polarity so that the duration of the galvanometric deflection is brief and practically indicates the speed of the wave if the muscle thickness is known or the muscle thickness if the speed of the wave is known When the impulse reaches B (fig 3 01e) the whole muscle block AB has a negative collective

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surface if recovery has not yet commenced at A and there is no potential difference between A and B Within a short time however recovery begins at A (fig 3 01f) and the cells become repolarised their collective surfaces becoming positively charged again While the recovery process or regression wave as it is called is spreading from A towards B a current again flows through the galvanometer but in the opposite direction The regression wave travels at the same speed as the accession wave, but causes a slower change of polarity, so that the galvanometric deflection is not so brief If the movements of the galvanometer are graphically recorded the passage of an excitatory impulse from A to B results therefore in a diphasic curve such as that shown in figure 3 02, the first deflection being quick or sharp the second slow or blunt Moreover if the neuro muscular tissue is uniform in all relevant respects the area occupied by the first deflection which may be measured by means of a planimeter with suitable magnification is exactly equal though of opposite sign to the area occupied by the second deflection In modern electrocardiographic parlance the first deflection is represented by the P wave when it reflects atrial excitation and by the QRS complex when it reflects ventricular excitation while the second is represented by the Ta and T waves respectively The QRS complex is written as the accession wave flows through the heart muscle from endocardial to epicardial surfaces not as the excitatory impulse passes down the bundle of His bundle branches and Purkinje network As the heart is not a uniform muscle block but a bi ventricular organ composed of numerous intertwining S shaped muscle bundles (Robb and Robb 1938) the initial ventricular deflection (QRS) is not monophasic as in figure 3 02 but complex and usually biphasic or triphasic nor is the second ventricular deflection (T) of equal area and opposite sign On account of this complexity, it is impossible in the light of present knowledge to determine by scientific theory precisely what an electrocardiogram should look like *it is only possible to find out by the practical method* For this reason electrocardiography has largely remained an empirical study

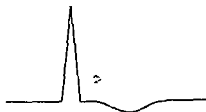


Fig 3 02—The diphasic curve produced by the processes of excitation and recovery in heart muscle

Einthoven s string galvanometer consists of an exceedingly fine fibre such as silver coated glass suspended between the poles of an electro magnet when a current passes through the fibre the latter is deflected towards one or other pole according to the direction of the current By suitable magnification and illumination the movements of the shadow of this string may be recorded on a moving photographic film Valve amplifying oscillographs of various forms operated by potential differences may be used instead of Einthoven s instrument Time marking is so arranged that fine vertical lines appear on the film at inter-

0 04–0 05 second, preferably with thicker lines every 0 20 second Horizontal lines for measuring voltage are spaced at intervals of 1 mm

Practical points to bear in mind include satisfactory insulation of the machine and lead wires to prevent 50 cycle A C interference proper standardisation of the galvanometer so that a deflection of 1 cm represents a potential difference of 1 mv and the elimination of skin resistance by means of electrode jelly The paste described by Jenks and Graybiel (1935) has proved effective it consists of sodium chloride 2950 G (6 5 lb) powdered pumice 3600 G (8 lb) gum tragacanth 226 G (8 oz) potassium bitartrate 114 G (4 oz) glycerol 710 ml (24 oz) phenol 28 5 G (1 oz) and water to 7 5 litres (2 gallons) The electrolytes are dissolved in one gallon of water while the gum and glycerol are heated for six hours in the other the two are then mixed stirred and reheated for one hour Phenol and pumice (and more water if necessary) are then added and mixed until the preparation has the consistency of cream Fresh soft green soap (B P) is very little inferior especially after rubbing the skin with some abrasive (Bell Knox and Small 1939) A number of satisfactory pastes or gels are marketed

## CHEST LEADS

Analysis of electrocardiograms has become simplified since the introduction of Wilson s neutral electrode (Wilson 1934) Previously all electrocardiograms were bipolar and registered the potential differences between two electrodes placed at different sites on the surface of the body each gathering different potential values According to Einthoven s theory however the algebraic sum of the potentials at the left arm right arm and left leg always equal zero these points representing the apices of an equilateral triangle in the frontal plane of the body the heart lying at its centre and the limbs being regarded as extensions of the lead wires * Thus it is only necessary to link up these three points to a common terminal (preferably through a resistance of 5 000 ohms in order to neutralise differences in skin resistance) to provide an electrode that remains at zero potential throughout the cardiac cycle If this neutral or indifferent electrode is linked to one arm of the galvanometer the instrument will record the potential variations of an exploring electrode linked to the other arm This is the basis of all V leads V standing for potential value or voltage at any particular point It has been agreed that positivity of this exploring electrode should be represented by an upright electrocardiographic deflection

It is now necessary to consider the variations in potential that may be recorded if the exploring electrode is placed over the surface of the left ventricle in man (Wilson *et al* 1944) As the accession wave spreads from endocardial to epicardial surfaces the left ventricular cavity (in contact with the tail of the wave) becomes electrically negative and the surface of the heart (in contact with the head of the wave) becomes electrically positive The galvanometer therefore records an upright or positive deflection R (fig 3 03b) When the accession wave reaches the surface the exploring

* The mathematical proof of this equation is given by Wilson *et al* (1946) Goldberger 1947) and by others

electrode undergoes an abrupt reversal of polarity and the galvanometer registers a sharp downward deflection (the intrinsic deflection) As both the cavity and surface of the left ventricle are then at the same negative potential the electrical field is abolished and the galvanometer comes to rest (fig 3 03c) A complication arises however, because the accession wave starts at some point (such as the left side of the interventricular septum) remote from the muscle underlying the electrode The left ventricular cavity thus becomes negative before the muscle under the electrode

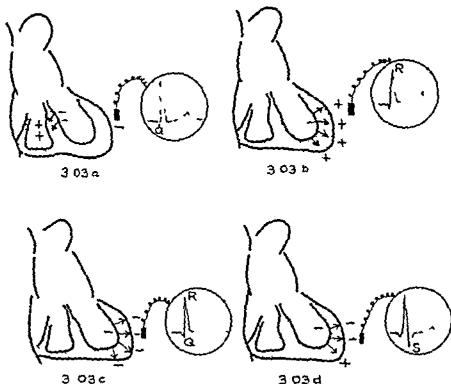



Fig 3 03—Formation of the Q R and S waves (see text)

begins to be actuated and this negative potential is passively transmitted to the surface to be recorded as an initial downward deflection Q (fig 3 03a) Since leads taken from the right ventricular cavity show an initial positive deflection in practically all instances it is believed that the excitation wave starts on the left side of the septum Again if the accession wave is still spreading through muscle remote from the exploring electrode when the galvanometer has registered the local intrinsic deflection the electrical field is maintained and continued negativity of the cavity is passively transmitted to the surface under the electrode to be recorded as a final downward deflection S (fig 3 03d)

When the exploring electrode is placed over the right ventricle similar principles hold good but the right ventricle is much thinner than the left→

and therefore the local potential differences are smaller and are normally overpowered by left ventricular events An initial R wave is almost invariable and represents the positive potential produced in the right ventricular cavity as the accession wave spreads through the septum from left to right, in other words it is the head of the left ventricular Q wave Further development of R as excitation passes through the anterior wall of the right ventricle is more or less prevented by the stronger negative potential induced by the tail of the accession wave that is spreading through the left ventricle this is represented by a large S wave Q is never seen over a normal right ventricle The second ventricular deflection T is upright over the left ventricle but may be inverted over the right (in leads $V_1$ and $V_2$)

With the aid of unipolar intramural electrodes Prinzmetal and his colleagues (1953) have proved that the inner third of the myocardium is electrically silent as if the Purkinje network penetrated to this depth Subendocardial leads always yield monophasic QS waves and R only begins to develop when the electrode is nearly half way between endocardial and epicardial surfaces As the electrode approaches the surface R increases rapidly in amplitude while S diminishes

In clinical electrocardiography multiple chest leads are designated leads $V_{1-}$ The figures indicate the position of the proximal electrode with reference to the chest wall and represent respectively the right and left borders of the sternum the left para sternal and mid clavicular lines and the anterior mid and posterior axillary lines, at the level of a line passing from the fourth intercostal space at points 1 and 2 to the fifth intercostal space at point 4 and thence horizontally (fig 3 04) For routine purposes leads $V_1$ $V_3$ and $V_5$ or $V_2$ $V_4$ and $V_6$ are usually sufficient but in particular instances other combinations or all seven leads are preferable A typical record obtained with this technique is illustrated in fig 3 05 Over the left ventricle ($V_5$ and $V_6$) there is a small Q wave a large R wave no S wave an iso potential R T junction and an upright T wave In the transition zone ($V_3$-$V_4$) Q has disappeared a conspicuous S wave has developed and T is sharply upright Over the right ventricle ($V_1$) there is again no Q wave, R is small S large and T is flattened In normal subjects the P wave is upright or occasionally diphasic (3 per cent) in $V_2$ but often diphasic (20 per cent) or inverted (15 per cent) in $V_1$ Q is usually present

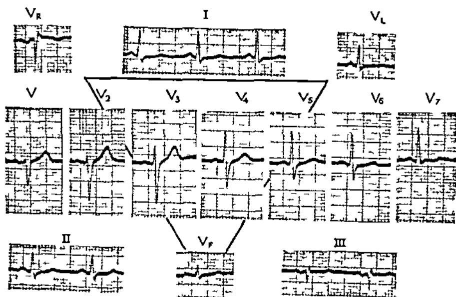
Fig 3 04—Multiple chest leads $V_1$-$V_7$ Position of the exploring electrode

$V_R$ I $V_L$

$V_1$ $V_2$ $V_3$ $V_4$ $V_5$ $V_6$

II $V_F$ III

(a) Average normal




(b) Clockwise rotation about longitudinal axis

Fig 3 05—Normal chest lead electrocardiogram

$V_R$ I $V_L$

$V_1$ $V_2$ $V_3$ $V_4$ $V_5$ $V_6$

II $V_F$ III

(c)—Anti clockwise rotation

Fig 3 05—Normal chest lead electrocardiogram (V –V )

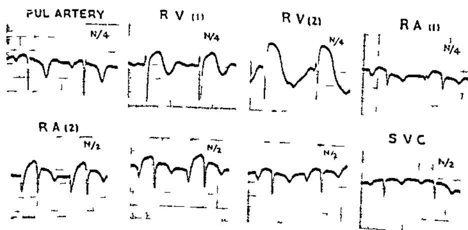



Fig 3 06—Right ventricular and pulmonary artery cavity leads

in $V_6$ occurs in $V_5$ in 45 per cent of cases but is rarely seen farther to the right S is usually absent in $V_{6-7}$ *is absent in* $V_5$ *in 17 per cent of cases*, but is invariably found in $V_3$ and $V_1$ T is always upright in $V_4$–$V_6$ may be occasionally diphasic in $V_3$ and is inverted in $V_1$ in 62 per cent of cases

If there is clockwise rotation about the longitudinal axis (viewed from below) the anterior surface of the septum is shifted to the patient s left this means that S is dominant in $V_4$ the transition zone being shifted to $V_4$ or $V_5$ In such cases Q may not appear until $V_6$ or $V_7$ Similar graphs are obtained when the heart is horizontal in position the septum then being displaced to the patient s left (fig 3 05b)

Anticlockwise rotation about the longitudinal axis brings the anterior surface of the septum to the patient s right The QR pattern may then be seen from $V_6$ to $V_3$ and the transition zone is shifted to V (fig 3 05c)

In addition to leads $V_1$–V other positions of the exploring electrode have been used with advantage under exceptional circumstances An *œsophageal lead may also be helpful in doubtful cases of posterior myo cardial infarction* and an intracardiac lead may provide interesting infor mation but these are rarely necessary for clinical purposes

*The œsophageal lead* takes its potential from the surface of the left atrium when high and from the posterior surface of the left ventricle when low Left atrial potentials are transmitted from the cavity of the left ventricle and show monophasic Q waves and inverted T waves the cavity of the left ventricle being negative throughout the inscription of the initial and second ventricular deflections The posterior surface of the left ventricle gives rise to a QR complex similar to that obtained anteriorly or laterally Œsophageal patterns therefore show monophasic Q waves or QR deflec tions Q dominating when the electrode is relatively high up R when the electrode is relatively low down T is usually negative when the electrode is high positive when low

*Intracardiac leads* from the cavity of the right ventricle show a small initial R wave followed by a deep S wave as already described If the catheter is passed through a patent foramen ovale into the left ventricle a monophasic Q wave is obtained When the catheter is passed into the pulmonary artery the small R wave seen within the cavity of the right ventricle disappears in favour of a monophasic Q wave (fig 3 06) this is because the pulmonary artery takes its potentials from the surface of the left auricle

There are thus only a limited number of basic QRS patterns upon which all ventricular deflections encountered in clinical electrocardiography de pend (fig 3 07) the QR complex of a left ventricular surface lead (T normally upright) the RS complex of a right ventricular surface lead (T usually upright) the monophasic Q wave of a left ventricular cavity lead (T normally inverted) the RS complex of a right ventricular cavity lead (T normally inverted) and the balanced QR pattern of a combined left

ventricular cavity and surface lead from the back of the heart (Goldberger 1947)

The direction of the second ventricular deflection T is opposite to theoretical prediction in all the basic patterns and suggests that the

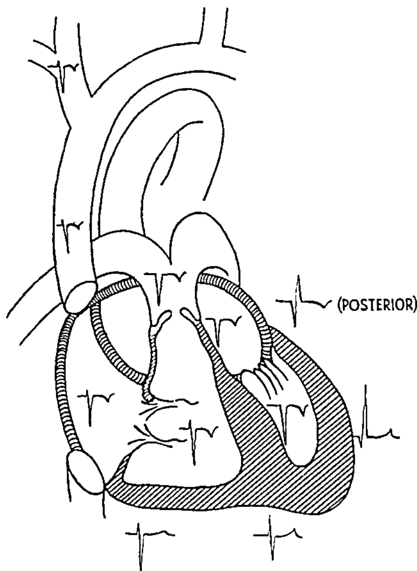



Fig 3 07—The basic QRS T patterns

recovery wave starts at the surface of the ventricles and is directed towards the cavities

Instead of V leads many workers including Wolferth and Wood (1932–33) who re introduced chest leads to clinical electrocardiography have coupled the exploring electrode with a relatively indifferent electrode

placed on the right arm (CR) or on the left leg (CF) Agreement will never be reached as to which of these is the more informative and it is expected that they will both be abandoned in favour of V leads They will be considered in greater detail in subsequent paragraphs

## UNIPOLAR LIMB LEADS

The potential values in the right arm ($V_R$) left arm ($V_L$) and left leg ($V_F$) may be obtained by placing the exploring electrode on the desired limb and linking it with Wilson's neutral electrode As unipolar limb leads are of low voltage it is customary to alter the standardisation so that a potential difference of 1 millivolt causes a deflection of 15 mm (instead of 10 mm) Alternatively Goldberger's augmented leads may be used With *this technique the V lead is attached to the limb the potential values of* which are being measured whilst the wire connecting this limb with the central neutral terminal is detached and left hanging free The potentials are thus increased by 50 per cent (Goldberger 1942) thus

$$\text{Since } V_R+V_L+V_F=O$$
$$\text{then } V_L+V_F=-V_R$$

Now when an electrode on the right arm is paired with a central terminal linked to the left arm and left leg the galvanometer records $V_R-\frac{V_L+V_F}{2}$ the latter being the mean potentials of the left arm and left leg

$$\text{Now}\quad V_R-\frac{V_L+V_F}{2}$$
$$=V_R-\frac{(-V_R)}{(\ 2\ )}$$
$$=V_R+{}^{1}V_R=1^{1}V_R$$

There has been some confusion concerning the equation $V_L+V_R+V_F$ = zero This statement is obvious in relation to the technique used for obtaining the unipolar limb lead potentials for the neutral electrode (e) employed with this technique is the mean of the potential values in each of the three limbs i e $e=\frac{L+R+F}{3}$

$$\text{Now } V_L=L-e$$
$$V_R=R-e$$
$$V_F=F-e$$
$$\text{So that } V_L+V_R+V_F=L+R+F-3e$$
$$=L+R+F-\frac{3(L+R+F)}{3}$$
$$=\text{zero}$$

It should be readily appreciated that this self evident fact has no bearing on whether the common terminal is neutral or otherwise but would be true for any value of e Thus the statement does not imply the truth of

Einthoven's hypothesis nor the validity of the theory underlying Wilson's neutral electrode

(Unipolar limb leads are useful in determining the electrical position of the heart in explaining the difference between CR CF and V chest leads and in demonstrating the basis of the standard leads $V_R$ usually shows inversion of all complexes because it reflects the negative potential of the cardiac cavities transmitted through the great vessels (figs 3 07 and 3 08)

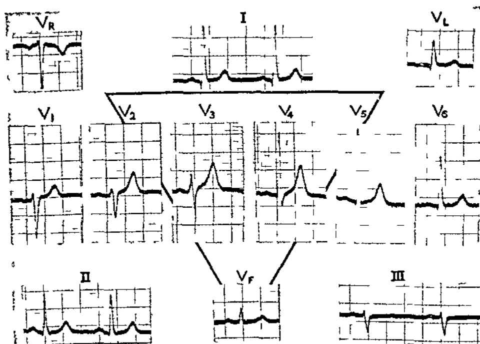



Fig 3 08— Unipolar limb leads ($V_L$ $V_R$ $V_F$) and standard leads 1 2 and 3
(a) Normal (the heart is more horizontal than vertical)

When the heart is normal in size and position $V_L$ and $V_F$ are mainly positive dominant left ventricular surface potentials being transmitted more or less equally to both of them (fig 3 08a) When the heart is electrically horizontal however left ventricular surface potentials are transmitted more strongly to the left arm and right ventricular surface potentials to the left leg There is then a small Q and tall R wave in lead $V_L$ and a small R and deep S wave in lead $V_F$ (fig 3 08b) When the heart is electrically vertical the negative potentials of the cavities are transmitted more strongly to the left arm and the left ventricular surface potentials more strongly to the left leg There is then a small R and deep S wave in $V_L$ and a small Q and tall R wave in $V_F$ (fig 3 08c) In normal subjects the electrical position of the heart is more or less in line with its anatomical position

Fig 3 08 (b)—Horizontal heart

Fig 3 08 (c)—Vertical heart

The differences between CR, CF and V chest leads may now be appreciated CR leads are V leads minus the potentials in $V_R$ whilst CF leads are V leads minus the potentials in $V_F$ As $V_R$ potentials are negative their subtraction from V in CR records makes all deflections more positive – not only is R taller in lead $CR_1$ but T is invariably upright in adults and in children over eight years of age Again since $V_F$ potentials are normally positive their subtraction from V in CF records makes all deflections more negative As the voltage is usually higher in $V_R$ than in $V_F$ however, CR leads show greater differences from V leads than do CF leads

## STANDARD LEADS

Einthoven s bipolar leads introduced at the beginning of the century and adopted as the standard leads throughout the world consist of the left and right arm (lead I) the left leg and the right arm (lead II) and the left leg and left arm (lead III) Electrocardiograms derived from these leads can be calculated of course from the deflections obtained with unipolar limb leads for lead I equals $V_L - V_R$ lead II equals $V_F - V_R$ lead III equals $V_F - V_L$ The subtraction of the negative potentials in $V_R$ from the positive potentials in $V_L$ and $V_F$ result in strongly positive QRS and T deflections in leads I and II Again as the voltage of R in $V_F$ is usually higher than that in $V_L$ QRS is also normally positive in lead III

By definition there is an obvious relationship between the three standard leads

$$\text{lead II} = \text{lead I} + \text{lead III}$$

This merely states that

$$V_F - V_R \text{ (lead II)} = V_L - V_R \text{ (lead I)} + V_F - V_L \text{ (lead III)} = V_F - V_R$$

and has nothing to do with Einthoven s theory or triangle

The relationship between the standard leads and the Wilson unipolar limb leads is as follows

$$V_L = \frac{I - III}{3}$$

$$V_R = \text{minus } \frac{I + II}{3}$$

$$V_F = \frac{II + III}{3}$$

The augmented values obtained with Goldberger s technique may be derived from the standard leads by changing the denominator in the above equations from 3 to 2

## NORMAL APPEARANCES

(Fig 3 08)

*P wave*

P represents the excitation process as it spreads from the sinoauricular node through both atria It is usually blunt and is upright in leads I and

II but may be inverted in lead III Its height should not exceed 2 0 mm and its duration 0 1 second Following P slight depression of the base line sometimes hidden by the QRS complex may be evident and represents atrial recovery or repolarisation It has been termed the atrial T wave or Ta wave

*P–R interval*

No deflection is caused by the passage of the excitatory impulse down the bundle of His its main branches and Purkinje network so that there is an iso potential interval between atrial and ventricular events this is the P–R interval and is conveniently measured from the beginning of P to the beginning of QRS It commonly ranges between 0 12 and 0 20 second but occasionally even in young subjects it may measure 0 21 or 0 22 second without evidence of heart disease or of general ill health

The P–R interval is little affected by spontaneous variations in heart rate but may be slightly reduced by atropine and slightly lengthened by carotid sinus compression Vagal tone has a much greater effect on the sinus node than on A–V conduction

*The QRS complex*

Q R and S when all are present form a triphasic complex representing the spread of the accession wave through the ventricles and are convenient symbols for describing the shape of the initial ventricular deflection Each is applied to a wave so defined by its direction and by its time relationship to the others Thus any upward deflection is called R or if there are two such R and R A downward deflection is called Q if it precedes R or if it is the only wave present and S if it follows R

Q rarely measures more than 1 or 2 mm in leads I and II and is often absent altogether in lead III, however, it may be conspicuous and may measure up to one third of the amplitude of R R should exceed 5 mm in height in the most favourable lead unless the spatial vector is unusually postero anterior Slight notching or slurring near its base is common and has no significance Distortion of the apex of R is rare in normal subjects but may be disregarded when unaccompanied by other changes S is variable, and is greatly influenced by axis deviation which will be considered later

The whole QRS complex should not exceed 0 1 second in duration and rarely exceeds 0 08 second in normal individuals

*RS–T segment*

This refers to that short segment between the QRS complex and the T wave i e between the end of the excitatory and the beginning of the recovery processes In some cases this is so short as to represent merely the RS–T junction Any deviation of the RS–T segment from the iso potential

base line should be regarded with suspicion Slight deviation of the order of 0 5 mm. may be within normal limits yet taken in conjunction with other findings may be highly significant

It is customary to include the proximal portion of the T wave when describing the shape of the RS–T segment e g whether concave, straight or convex Speaking in this way a normal RS–T segment curves gently from its point of origin in the direction of the T wave it is neither straight, nor does it deviate in the opposite direction first

*T wave*

T represents the recovery process or the regression wave (repolarisation) and is known as the second ventricular deflection It is normally upright in leads I and II but may be inverted in lead III It should measure at least 2 mm in amplitude in the most favourable lead

*Q–T interval*

The interval between the beginning of QRS and the end of T represents the total time occupied by ventricular excitation and recovery It is inversely proportional to the heart rate ranging between 0 42 second at a speed of 48 per minute and 0 28 second at a speed of 110 The formula of Bazett (1920) is $Q\text{–}T=K\sqrt{C}$ where C represents the cycle length The constant K is variously given as 0 38—0 39 plus or minus 0 04 and is a trifle longer in women than in men and children

Taran and Szilagyi (1947) have made the sensible suggestion that the Q–T interval should be recorded as corrected for rate i e as $Q\text{–}T_c$ This should equal Bazett s constant K i e the actual Q–T interval when the heart rate is 60 per minute or when the cycle length is one second $Q\text{–}T_c$ is easily calculated with the aid of a slide rule when the actual Q–T interval and cycle length are known for $Q\text{–}T$ (or $K$)$=\frac{Q\text{–}T}{\sqrt{C}}$ The Q–T interval is lengthened by hypocalcæmia (fig 3 33) and shortened by digitalis (fig 3 27b) $Q\text{–}T_c$ may be prolonged in active rheumatic carditis (Taran and Szilegyi 1947) There is some evidence that Q–T is also lengthened by cardiac enlargement from any cause and shortened by cardiac compression as in pericardial effusion (Van Lingen 1947)

*U wave*

Following T and coinciding with the super normal recovery phase a small rounded positive deflection the U wave may be seen Its significance is not fully understood but it appears to be exaggerated in chest leads taken from the right of the interventricular septum and to be flattened or even inverted in leads taken from the left of the septum when there is left ventricular hypertrophy and vice versa when there is right ventricular hypertrophy It may also be inverted in left ventricular surface leads during an attack of angina pectoris It is accentuated by digitalis

## THE CARDIAC VECTOR

Maximum potential differences within the heart at any given moment may be represented in magnitude and direction by a line of appropriate length and spatial direction (drawn from the hypothetical centre of electrical events) which may be called a vector and its direction a spatial axis Both magnitude and direction of this vector alter from moment to moment during the phases of ventricular excitation and recovery but may be resolved into mean values If such a vector is projected on to the frontal plane of the body its new momentary or mean manifest value may be calculated by suitable measurements, detailed below of the electrocardiograms obtained from any two of Einthoven s leads for the frontal plane or manifest vector may be projected on to the sides of an equilateral triangle the apices of which are represented by the left and right arms (or shoulders) and by the left leg (or symphysis pubis) the sides of the triangle thus representing the three standard leads For example if the line AB (fig 3 09) represents the maximum momentary manifest QRS vector i e if it

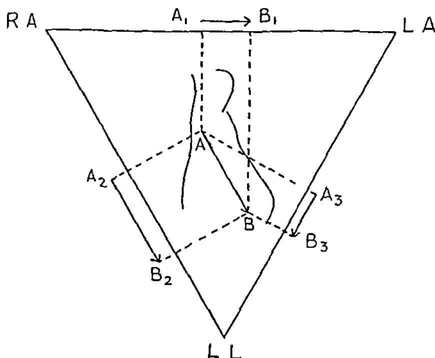



Fig 3 09—Projection of the frontal plane QRS vector on to the sides of Einthoven s equilateral triangle

represents the projection on to the frontal plane of the body of a line in space representing the magnitude and direction of maximum potential differences generated within the heart during the period of ventricular excitation then the lines A1–B1 A2–B2 and A3–B3 obtained by projecting the line AB on to the sides of Einthoven s equilateral triangle give the magnitude and direction of the maximum QRS deflection in leads I II and III respectively Moreover it can be easily shown that at any given moment the amplitude of the QRS deflection in lead II equals the algebraic sum of that in leads I and III or the amplitude of the QRS deflection in any one lead equals the algebraic sum of that in the other two The same law applies to atrial activity and to the recovery phase i e to the P Ta and T waves and to mean as well as momentary values Conversely if the magnitude and direction of the QRS complex at any given moment is known in any two leads their resultant drawn from the centre of Einthoven s triangle represents the manifest (frontal plane) vector of QRS at that particular moment and its direction the manifest electrical axis In current electrocardiographic nomenclature the electrical axis refers to this resultant frontal plane axis as obtained from the maximum upright QRS deflection in any two leads if apparently synchronous and is expressed in terms of its angle with the horizontal being plus when rotated clockwise from this base minus when anti clockwise As so expressed the normal electrical axis lies between 0 and 90 degrees and has a wider range than the frontal plane anatomical axis

*Triaxial reference system*

For convenience Einthoven s triangle may be suitably represented as a triaxial reference system (Bayley 1943) The lines representing the three sides of the triangle are transposed so that they intersect at a common point O (fig 3 10) The horizontal line RL then represents lead I and the

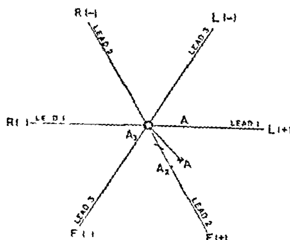



Fig 3 10—Bayley s triaxial reference system

lines RF and LF leads II and III respectively The customary signs are preserved so that R is negative L positive and L negative or positive as shown in the diagram If the vector OA, is projected on to these lines its value in the standard leads may at once be determined by the lengths OA1, OA2 and OA3 The converse may be applied with equal simplicity

By measuring the net area of QRS in any two leads (instead of momentary synchronous points) by means of a planimeter and suitable magnification (or by dividing the amplitude of the wave by half its width) the area below the base line being subtracted from that above the resultant mean axis of QRS in the frontal plane can be determined in similar fashion (Wilson *et al*, 1934) Measurements may be made in millivolt seconds microvolt seconds or in suitable units based on voltage×time (Ashman and Byer 1943) Such a resultant drawn from the centre of Einthoven s triangle having both magnitude and direction, is called the mean QRS vector in the frontal plane or the manifest mean QRS vector and its direction the manifest mean QRS axis Manifest mean vectors for T and P may be similarly obtained Bayley (1943) has suggested that the symbol A might well designate the axis of such vectors and the symbol A their magnitude the manifest mean axis of QRS would then be called $\hat{A}_{QRS}$ and its magnitude $A_{QRS}$

If the heart were a simple uniform muscle block the algebraic net area occupied by QRS and T would be zero as it is not the net area of QRST has a positive or negative value which if measured in any two leads may be resolved into a vector drawn from the centre of Einthoven s triangle The axis of this vector or the manifest mean QRST axis ($\hat{A}_{QRST}$) has been called the ventricular gradient (Wilson Macleod and Barker 1931) or G and its magnitude G The gradient represents the magnitude and direction of maximum local variations in the speed of the processes of excitation and recovery whereby the heart differs from a uniform muscle-block

The manifest mean axis of QRS averages about 60 degrees that of T about 50 degrees The ventricular gradient in hearts which are not anatomically rotated ranges between 45 and 65 degrees On the whole hearts which are relatively central in position i e rotated clockwise (viewed from the front) about their antero posterior anatomical axis are also rotated clockwise (viewed from the apex) about their longitudinal anatomical axis and show clockwise deviation i e deviation to the right of all manifest momentary and mean electrical axes, but the greatest shift occurs with the ordinary momentary electrical axis of QRS and the least with the ventricular gradient This also applies to transverse hearts with anti clockwise rotation and deviation of all electrical axes to the left (Ashman and Byer 1943)

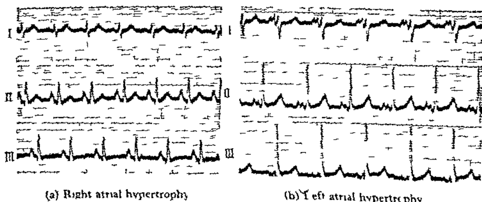
From what has been said it should be clear that the QRS and T vectors in the frontal plane of the body alter in magnitude and direction from moment to moment during the phase of ventricular excitation and recovery As one end of such a vector is fixed at the centre of Einthoven s triangle it follows that the other end must describe a continuous curve Mann (1920)

showed how such curves could be reconstructed and later devised a method of recording them directly (1931) More recently Wilson and Johnston (1938) employing the cathode ray oscillograph published typical curves and called them vectorcardiograms Even these however are restricted to the behaviour of the vector in the frontal plane of the body being so limited by use of the standard limb leads Wire models of spatial vectorcardiograms have been constructed by Duchosal (1949)

## ELECTROCARDIOGRAPHIC ABNORMALITIES

### ABNORMALITIES OF THE P WAVE

There are four main varieties of P wave deformity the tall sharp P wave of right atrial hypertrophy (fig 3 11a) the conspicuous widened P wave of left atrial hypertrophy which may be bifid rounded or flat topped (fig




(a) Right atrial hypertrophy (b) Left atrial hypertrophy

Fig 3 11—Abnormal P waves

3 11b) the low voltage widened P wave which may be also bifid rounded, or flat topped (fig 3 11c) and the inverted P wave (fig 3 11d)

Tall sharp P waves are characteristic of pulmonary hypertension pulmonary stenosis and tricuspid stenosis The voltage ranges between 2 and 5 mm and as the wave is not widened it becomes peculiarly sharp like an arrowhead They are usually most evident in leads II and III

Conspicuous widened P waves measuring 0 12 second in duration are almost diagnostic of mitral stenosis The voltage may be normal or slightly increased but rarely exceeds 2 5 mm Most examples are bifid the first peak representing right atrial activity the second left atrial activity so that the P mitrale implies delay in left atrial activation (Reynold 1953) They are usually seen best in leads I II and V

P waves similar in shape and width but usually of lower voltage may be seen sometimes in advanced cases of hypertensive heart disease or aortic valve disease It is uncertain whether they represent left atrial

dilatation due to left ventricular failure as originally suggested by Wood and Selzer (1939) or inter atrial block (Berconsky and Kloztman 1945)

Inverted P waves are found in lead I in cases of dextrocardia in leads II and III in coronary sinus rhythm and in all leads in many cases of nodal rhythm




Fig 3 11 (c)—P waves in hypertensive heart failure

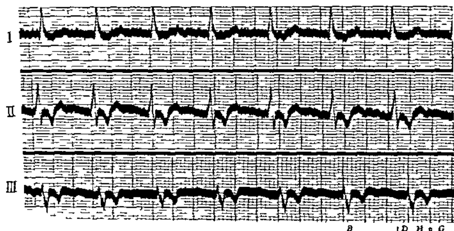



Fig 3 11 (d)—Inverted P waves in nodal rhythm

## ABNORMALITIES OF THE QRS COMPLEX

### *Axis deviation*

It has already been pointed out that the electrical axis of the heart refers to the frontal plane projection of the maximum momentary spatial vector and usually lies between 0 and 90 degrees more or less in the anatomical axis Anti clockwise rotation of the heart about its antero posterior axis (viewed from the front) or about its longitudinal axis (viewed from the

cardiac apex) causes deviation of the electrical axis to the left, so that the frontal plane vector may make a minus angle with the horizontal whilst clockwise rotation about similar axes causes right axis deviation the vector now making an angle of more than 90 degrees with the horizontal Left or right axis deviation respectively also occurs when the left or right ventricle is disproportionately enlarged Moreover left ventricular enlargement is often associated with anti clockwise rotation about both anatomical axes and right ventricular enlargement with clockwise rotation

Reference to Einthoven s triangle will show that if the electrical axis deviates to the left and approaches or surpasses the horizontal lead I becomes the axial lead (fig 3 12) $R_I$ then carries the maximum voltage $R_{II}$ is smaller and the maximum QRS deflection in lead III is downwards, i e the main deflection is S In such cases $S_{III}$ is really the electrical counterpart of $R_I$ Unipolar limb leads commonly show an electrically horizontal heart R in $V_L$ and S in $V_F$ being unusually conspicuous

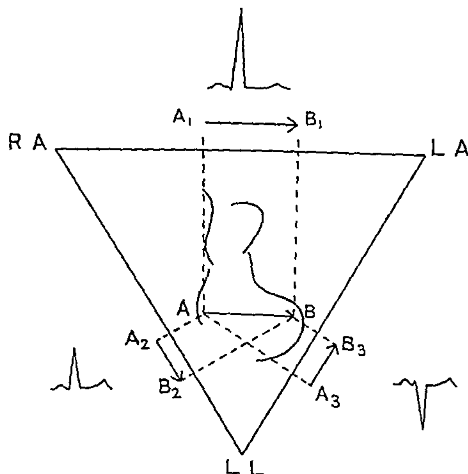



Fig 3 12—Left axis deviation (Einthoven s triangle)

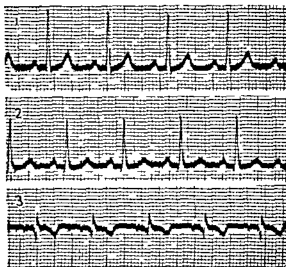



Fig 3 13—Axis deviation due to elevation of the diaphragm ($Q_3$ $S_1$ type)

Left axis deviation occurs in 10 per cent of normal individuals, in any condition in which the left ventricle is disproportionately enlarged in cardiac displacement to the left from scoliosis or from intrathoracic causes and when the diaphragm is elevated causing the heart to lie more transversely It may not be possible from examination of the limb lead QRS complexes alone to decide whether axis deviation is due to displacement or to left ventricular preponderance but this distinction may often be made by considering the behaviour of the RS-T segment and T wave and especially by noting the QRS pattern in multiple chest leads (*vide infra*)

A particular form of axis deviation is seen with elevation of the diaphragm as from obesity pregnancy flatulence or ascites $R_I$ is taller than $R_{II}$, $S_I$ and $Q_{III}$ are prominent and $T_{III}$ is inverted (fig 3 13) In such cases there is no Q wave in lead $V_F$ and the T wave usually remains inverted in lead $V_1$

When the electrical axis is deviated to the right so that it occupies a more or less vertical position lead III becomes the axial lead (fig 3 14) $R_{III}$ then carries the maximum voltage $R_{II}$ is smaller whilst the maximum deflection in lead I is S which is the electrical counterpart of $R_{III}$ In unipolar limb leads S is conspicuous in $V_L$ and R in $V_F$ Right axis deviation is the rule in newly born infants is common in very young children occurs in 1 per cent of normal children over the age of eight,

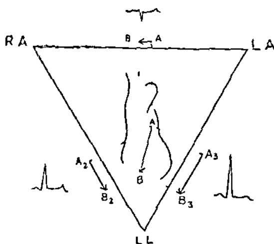



Fig 3 14—Right axis deviation (Einthoven s triangle)

and is rarely seen in strictly normal adults It may be caused by appropriate cardiac displacement or rotation, and by right ventricular dominance As with left axis deviation it may not be possible from inspection of the limb lead QRS complexes alone to determine whether the axis shift is due to right ventricular dominance or otherwise but the behaviour of QRS in multiple chest leads may clarify the issue (*vide infra*)

*Left ventricular preponderance*

When the left ventricle is enlarged the accession wave takes longer to penetrate that chamber and creates more powerful potential differences Thus R in leads $V_5$ and $V_6$ and S in leads $V_1$ and $V_2$ have a larger amplitude (R in $V_{4, 5, \text{ or } 6} > 25$ mm S in $V_1 > 15$ mm) the intrinsic deflection in left ventricular surface leads is delayed (longer than 0 05 second) and the width of QRS slightly increased (0 1 second) Secondary changes in the T wave occur in advanced cases the R T segment being depressed

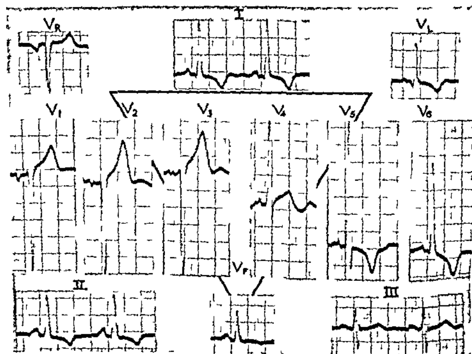



Fig 3 15—Left ventricular preponderance

and T inverted in leads $V_5$ and $V_6$ and the S T segment being elevated and T sharply upright in leads $V_1$ and $V_2$ (fig 3 15)

When the heart is horizontal which is usual $V_L$ resembles $V_5$ and $V_F$ resembles $V_1$ both in respect of QRS and T The appearances in standard lead I therefore also resemble $V_5$ or $V_6$ and those in lead III resemble $V_1$

When the heart is more or less vertical which is less common left ventricular surface potentials are transmitted more to the left leg There is then no axis deviation in standard leads (Wilson 1944) but high voltage and perhaps T wave inversion in all (fig 3 16) Concordant left ventricular preponderance as it is called is best seen in concentric left ventricular hypertrophy such as may occur in aortic stenosis and malignant hyper tension

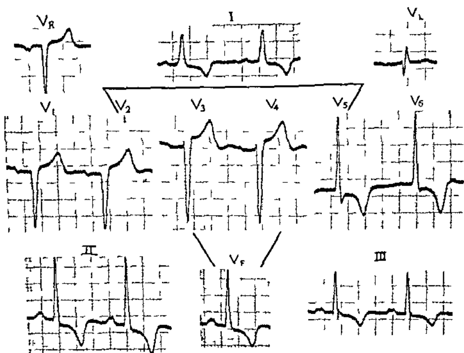



Fig 3 16—Left ventricular preponderance (heart semi vertical)

*Right ventricular dominance*

When there is gross enlargement of the right ventricle the potential differences generated by the wall of that chamber may approach or even surpass those from the left ventricle Right ventricular surface leads may then truly represent the outward spread of the accession wave beneath the exploring electrode After a small initial septal R wave a tall secondary R replaces the usual S wave in leads $V_1$ and V and S is conspicuous in $V_5$ and $V_6$ (fig 3 17) Secondary inversion of the T wave with slight depression of the R T segment is common in $V_1$ to $V_3$ In lesser degrees of right ventricular hypertrophy clockwise rotation about the longitudinal axis (viewed from below) is usually held responsible for the changes Thus the occasional appearance of Q in lead $V_1$ followed by a tall R wave may be derived from potentials at the back of the heart

As a rule the heart is also vertical in position $V_L$ is strongly influenced by negative cavity potentials and $V_F$ by left or right ventricular surface potentials In other words QRS is mainly negative in $V_L$ and strongly positive in $V_F$ Standard leads therefore show right axis deviation and

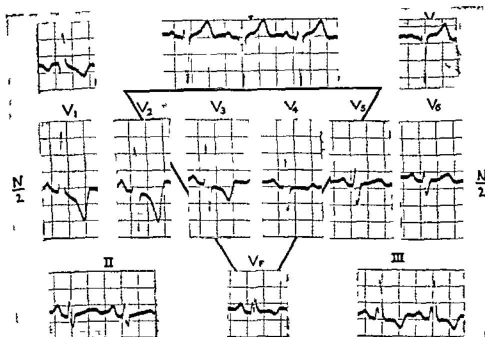



Fig 3 17—Right ventricular dominance (case of pulmonary stenosis)

there may be inversion of the T wave with depression of the R T segment in lead III or in leads II and III When R is dominant in $V_1$ and S in $V_5$ right axis deviation also occurs when the heart is horizontal for $V_L$ then reflects $V_5$ and $V_F$ reflects $V_1$

*Widening of the QRS complex*

The accepted maximum normal limit of 0 1 second for the duration of the QRS complex is generous and includes many instances of abnormal widening due to increased thickness of the ventricular walls As the accession wave causes almost instantaneous reversal of polarity in the tissue it excites the width of QRS depends almost entirely on the thickness of the ventricular walls provided the conducting system is normal and assuming that the speed of the wave is constant With extremely hypertrophied hearts it is theoretically possible for QRS to measure as much as 0 12 second in duration but in fact it rarely exceeds 0 1 second It is probably wise to regard anything over 0 11 second as intraventricular block It is found too that widening due to ventricular hypertrophy is usually associated with high voltage whereas in bundle branch block QRS is commonly

notched splintered or heavily slurred When the heart is grossly dilated there may be some delay in the passage of the excitatory impulse down the Purkinje network, causing intraventricular block Some such mechanism may account for the transient right bundle branch block that occurs occasionally in massive pulmonary embolism and for the right bundle branch block so commonly seen with atrial septal defect A Q wave can nearly always be demonstrated in suitable left ventricular surface leads when widening of the initial ventricular deflection is due to left ventricular hypertrophy whereas it is ordinarily absent in left bundle branch block

Widening of the QRS complex is also seen in uræmia when it is due to a raised blood potassium (figs 3 33 and 3 34)

*Bundle branch block*

In *left bundle branch block* the excitatory process spreads through the right ventricle in normal fashion but does not at first reach the left ventricle As the interventricular septum is excited from the right side the accession wave spreads through it from right to left The cavity of the left ventricle therefore becomes initially positive and this potential is transmitted passively to the surface as an R wave in $V_5$ or $V_6$ There can be no Q wave in such leads with a healthy septum When the accession wave reaches the left side of the septum there is an immediate reversal of polarity the left ventricular cavity becoming momentarily negative This negativity is again transmitted passively to the surface $V_5$ showing a momentary downward deflection following the initial R wave Almost immediately however, the excitatory process spreads throughout the endocardium of the left ventricle and the accession wave begins to flow outwards in the usual way The surface of the left ventricle then becomes actively positive and the true R wave is written When the surface is activated the final intrinsic downward deflection occurs $V_5$ or $V_6$ thus exhibits a large widened R wave interrupted by a relatively early notch representing the arrival of the accession wave at the left side of the septum (fig 3 18) Right ventricular surface potentials are influenced at first by a normal right ventricular accession wave and later by the delayed negativity of the cavity of the left ventricle which is passively transmitted through the depolarised septum and right ventricle Thus $V_1$–$V_3$ exhibit small R waves early intrinsic deflections and deep wide S waves The total duration of QRS commonly measures 0 12 to 0 16 second As the heart is usually horizontal the $V_5$–$V_6$ pattern is seen also in $V_L$ and lead I and the $V_1$ pattern in $V_F$ and lead III Should the heart be vertical however the $V_5$–$V_6$ pattern is transmitted to the left leg and the appearances in standard leads may be mistaken for right bundle branch block (fig 3 18b) Whatever the position of the heart in left bundle branch block deviation of the RS T segment and the direction of the T wave are usually of opposite sign to the main QRS deflection Thus with horizontal hearts the RS T segment is depressed and the T wave inverted in $V_5$–$V_6$ $V_L$ and standard lead I

VR I VL
V1 V2 V3 V4 V5 V6
II VF III

Fig 3 18 (a)—Left bundle branch block (heart horizontal)

VR I VL
V1 V2 V3 V4 V5 V6
II VF III

Fig 3 18 (b)—Left bundle branch block (heart vertical)

Left bundle branch block may occur in diseases chiefly affecting the left ventricle such as hypertensive heart disease aortic stenosis syphilitic aortic incompetence and ischæmic heart disease in non rheumatic myocarditis cardiac fibrosis and generalised cardiopathy of almost any type and occasionally in otherwise clinically normal hearts although far less commonly than right bundle branch block

*In right bundle branch block* the septum is activated entirely from the left side The potential of the right ventricular cavity is therefore initially positive and is passively transmitted to the surface where it may be recorded as the first part of R When the accession wave reaches the right side of the septum the polarity is abruptly reversed and a pseudo intrinsic deflection is recorded at the surface Almost at once however the right ventricular wall is invaded and the surface then becomes actively positive This results in a second R wave and finally in the true intrinsic deflection Leads $V_1$ and V therefore show a widened notched R wave or a large M complex T is in the opposite direction (fig 3 19a) Over the left ventricle in leads

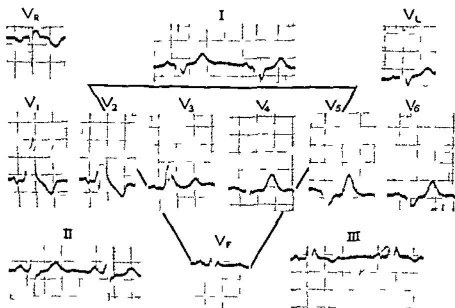



Fig 3 19 (a)—Right bundle branch block (heart horizontal)

$V_5$ and $V_6$ a normal QR wave and intrinsic deflection are followed by a grossly slurred S wave representing delayed negativity of the right ventricular cavity passively transmitted through the depolarised septum and left ventricle As a rule $V_5$ and $V_6$ potentials are transmitted to $V_L$ and form the pattern of standard lead I the M complex of $V_1$–V is usually seen in $V_F$ and in standard lead III When the heart is vertical however $V_1$

potentials may be transmitted to $V_L$ and standard leads may look like left bundle branch block (fig 3 19b) Multiple chest leads may be necessary not only to determine which bundle branch is blocked but also to detect the lesion at all in some cases partial right bundle branch block for instance is frequently overlooked in standard leads Right bundle branch

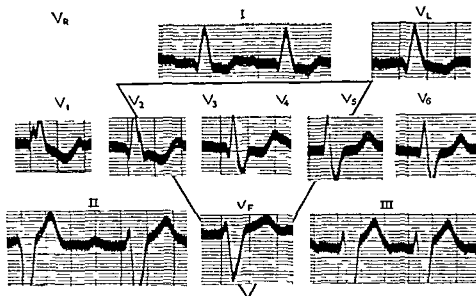



Fig 3 19 (b)—Right bundle branch block (heart vertical)

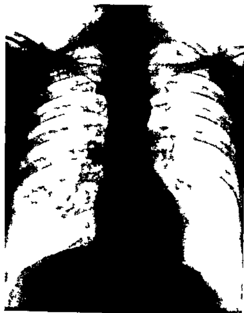
block may occur in any of the diseases that may result in great dilatation of the right ventricle particularly atrial septal defect and Ebstein s disease in ischaemic heart disease and any of the generalised cardiopathies such as isolated myocarditis and by no means rarely in otherwise normal hearts

## *ABNORMALITIES OF THE RS T SEGMENT AND T WAVE*

It is profitable to consider the RS T segment and T wave together and in many cases to consider them also in relationship to the QRS complex for they are all ventricular events The various patterns made up by these three variables in limb and multiple chest leads provide a wealth of information concerning the state of the ventricles in health and disease Secondary inversion of the T wave in relation to QRS changes has already been described

### *Myocardial infarction*

It is customary to describe two types of electrocardiogram associated with myocardial infarction $T_I$ and $T_{III}$ types (Parkinson and Bedford 1927) the first denoting anterior, the second posterior lesions (Barnes and



(a) Postero anterior view



(b) 1st oblique position (right anterior)



(c) 2nd oblique position (left anterior)

Fig 4 03—Teleradiogram of a normal subject

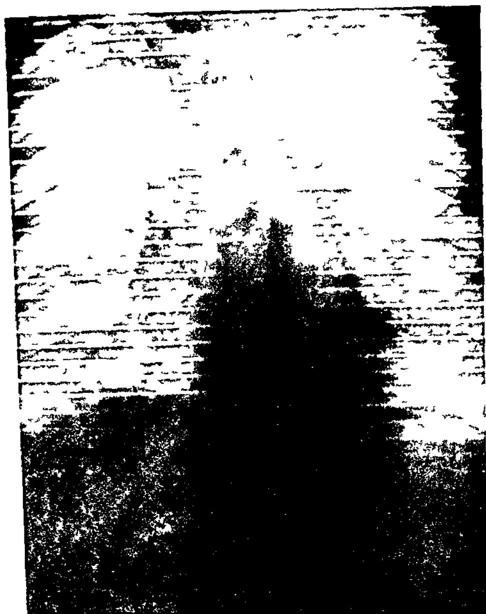


Fig 4 04—Normal kymogram (P A view)
*(By urtesy f Dr J er H k )*

Whitten, 1929) There is no essential difference in the shape of these two patterns, the difference depending upon the leads in which they are found

If an infarct involves the whole thickness of the muscle wall no accession wave can flow through it The negative cavity potential produced by outward spread of the accession wave through remote healthy muscle is then passively transmitted through the infarct to the surface overlying it An electrode placed over the infarct therefore registers a monophasic Q wave

If the infarct involves only the inner third of the myocardium no electrocardiographic changes occur for this zone is electrically silent (Prinzmetal *et al* 1953)

If the outer layers are patchily involved QR complexes occur at the epicardial surface the initial Q wave is due to transmission of the negative cavity potential and the subsequent R wave to spread of the accession wave through patches of live muscle in the outer layers (Prinzmetal *et al* 1954) R waves of this kind are usually of reduced voltage In anterior left ventricular infarcts these QRS changes may be registered in leads $V_3$ $V_4$ $V_5$ and $V_6$ being more marked in $V_3$–$V_4$ in antero septal infarcts and in $V_5$–$V_6$ in antero lateral infarcts They are commonly transmitted to $V_L$ and are therefore seen well in standard lead I (fig 3 20) Similar QRS changes occur in posterior infarcts but are transmitted to $V_F$ and thus to standard lead III (fig 3 21) When the heart is vertical however, typical changes in $V_5$ from an anterior infarct may be transmitted to lead $V_F$ and hence to standard leads II and III (fig 3 22)

According to Wilson *et al* (1933) partly necrosed muscle sets up a steady current due to the development of potential differences between

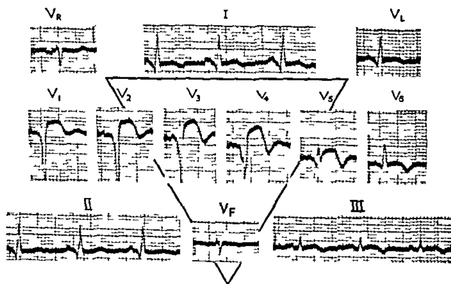



Fig 3 20—Anterior myocardial infarction showing pathological Q waves and elevation of the RS T segment in leads $V_{1-4}$ $V_L$ and standard lead I

VR I VL

V1 V2 V3 V4 V5 V6

II VF III

Fig. 3.21—Posterior myocardial infarction showing pathological Q waves and elevation of the RS-T segment in lead VF and standard leads II and III

VR I VL

V1 V2 V3 V4 V5 V6

II VF III

Fig. 3.22—Anterior infarction with vertical heart. Standard leads show changes that simulate those of posterior infarction

(a) Anterior

(b) Posterior

Fig 3 23—Later stages of anterior (a) and posterior (b) infarction showing typical Q waves and inversion of the T wave in appropriate leads

injured and healthy tissue Injured tissue is electro negative, healthy tissue is positive and completely necrosed tissue electrically inert When the injured area involves the outer portion of the ventricular wall the surface is therefore negative the current flowing from without inwards An electrode placed over the infarct registers this negativity by depressing the base line This is shown in the electrocardiogram by abrupt elevation of the ba e line when the current of injury is momentarily abolished by spread of the accession wave through the healthy tissue for such activation causes the healthy tissue to take up a negative potential and so abolishes the potential differences set up by the injury In other words superficial injury results in elevation of the RS T segment In anterior infarcts this displacement is seen in leads $V_3$-$V_6$ and is commonly transmitted to $V_L$ and hence to standard lead I (fig 3 20) In posterior infarcts it is seen in low œsophageal leads in $V_7$ and is transmitted to $V_F$ and hence to standard lead III (fig 3 21)

This classic theory has been challenged by Prinzmetal (1954) on the grounds that intramural electrodes from healthy myocardium adjacent to a fresh infarct do not show depression of the S T segment as they should do if there is a current of injury flowing across the boundary zone from the electrically negative injured tissue to electrically positive healthy muscle instead the S T segment from adjacent areas is normal Again the S T segment from surface electrodes overlying a subendocardial infarct is

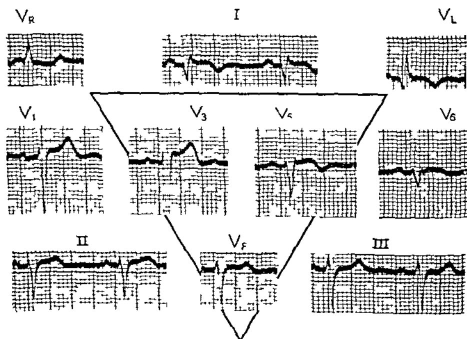



Fig 3 24—Anterior myocardial infarction showing an R wave which is smaller in $V_3$ to $V_5$ than in $V_1$

normal not depressed Elevation of the S T segment is always recorded when the intramural electrode is situated anywhere within the injured zone and is maximum at the centre Reciprocal depression occurs over the opposite wall of the ventricle

Pathological Q waves may be seen in acute cases within a few hours of the onset and usually outlast all other evidence of infarction often being permanent Elevation of the RS T segment occurs even earlier, but usually subsides within two or three weeks The shape of the segment is typical being straight instead of concave when initially elevated and being convex or cove shaped (Pardee 1920) when the RS T junction approaches or regains the iso potential level The T wave itself becomes inverted within a few days of the onset often profoundly so, reaching its greatest amplitude at about the same time that the RS T junction first regains the iso potential level (fig 3 23 a and b) Further changes are regressive but the appearances rarely revert to normal

In $T_1$ patterns reciprocal effects are usually observed in lead III i e the RS T segment may be depressed at first and T may be sharply upright later Again in posterior infarcts early RS T depression and later accentuation of the T wave may often be seen in lead I and in anterior chest leads A helpful sign of old anterior infarction is an R wave in $V_1$–$V_2$ which is taller than that in $V_3$–$V_4$ (fig 3 24) especially when the appearances in $V_5$–$V_6$ are more or less normal Finally it is most important to understand that characteristic changes may be found in multiple chest leads or in an œsophageal lead when the standard limb leads are normal and that a single chest lead may be normal when others show diagnostic features

*Pericarditis* In all types of generalised pericardial disease except hydropericardium superficial epicardial involvement may cause a current of injury to flow from the surface towards the underlying healthy muscle in other words the surface of the heart develops a negative potential The situation therefore resembles that in superficial myocardial infarction but the lesion is general instead of local Thus in the initial stages elevation of the RS T segment may be seen in all chest leads, in both $V_L$ and $V_F$ and therefore in all standard leads (fig 3 25a) Unlike most records of acute myocardial infarction the RS T segment remains concave As the underlying muscle is healthy there are no pathological Q waves After a few days the RS T segment regains the iso potential level and the T wave becomes inverted (fig 3 25b) Upward coving of the RS T segment does not occur If pericarditis is localised the changes described may be confined to corresponding leads but few important forms of pericarditis remain localised for long Serial records nearly always reveal what may be called the $T_{II}$ pattern in contrast to the $T_I$ or $T_{III}$ types of myocardial infarction Low voltage QRS complexes usually indicate pericardial effusion The electrocardiogram returns to normal as the pericarditis recovers

In *chronic constrictive pericarditis* flattened or inverted T waves

(a) Early stage showing elevation of the RS T segment in leads $V_4$–$V_6$, $V_F$ and all standard leads

(b) Late stage showing inversion of the T wave in all standard leads

Fig 3 25—Pericarditis

leads are permanent and are usually associated with low voltage QRS complexes (fig 3 26) Not infrequently the P waves are widened and relatively prominent

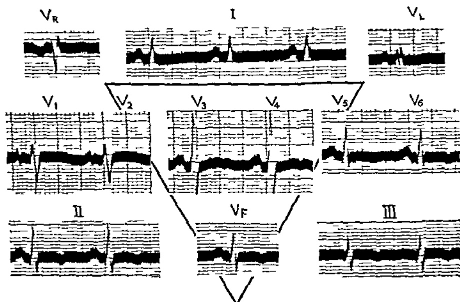



Fig 3 26—Chronic constrictive pericarditis showing low voltage and flat T waves

*Digitalis T wave pattern*

Digitalis depresses the RS T segment and shortens the Q T interval At first the RS T junction is depressed and there is gentle sagging of the RS T segment T remaining upright (fig 3 27a) In the second stage sagging is more marked and the peak of T can no longer be discerned In extreme digitalisation the RS-T segment becomes a straight line sloping downwards from its depressed origin to a blunt peak (fig 3 27b)

In normal hearts these effects are seen in all leads but especially in lead $V_5$ and standard lead II When the heart is electrically horizontal they are seen best in $V_5$ $V_L$ and standard lead I when it is electrically vertical they are best seen in $V_5$ $V_F$ and standard lead III When the left ventricle is enlarged and the heart horizontal the changes occur more markedly in $V_5$ $V_L$ and standard lead I and the RS T segment may be elevated and upwardly convex in $V_1$ $V_F$ and standard lead III When the right ventricle is enlarged they may be most conspicuous in $V_1$ $V_F$ and standard lead III and the RS T segment may be elevated and upwardly convex in $V_5$ $V_L$ and standard lead I

*Anoxic T waves*

Electrocardiograms taken from patients during an attack of angina pectoris may show transient depression of the RS T segment (fig 3 28)

(a) Showing sagging of the RS-T segment and shortening of Q-Tc to 0·33 second

(b) Showing gross depression of the RS-T segment or an inverted T wave with a straight proximal limb. Q-Tc is shortened to 0·36 second

*Fig. 3. 7*—*The effect of digitalis on the electrocardiogram* (a) slight (b) marked

Fig 3 28—Depression of the RS T segment during an attack of angina pectoris

with or without inversion of the U wave (fig 3 29) Similar records may be associated with carbon monoxide poisoning vasomotor syncope asphyxia and severe hæmorrhage In all these conditions there is myocardial hypoxia *In carbon monoxide poisoning the changes may last for a week or two* and there may be true T wave inversion (fig 3 30) Transient depression of the RS T segment in all leads may be induced in many normal individuals and especially in those with ischæmic heart disease by causing them to breathe 10 per cent oxygen (Levy *et al* 1938) Exertion may have a similar effect in patients with angina pectoris The depression has been attributed to a steady current of injury flowing from the inner layers of the myocardium towards the surface so that the base line of the electrocardiogram is positively displaced When the electrical field is momentarily abolished by the spread of the accession wave the base line temporarily subsides to its

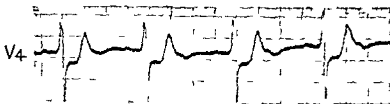



Fig 3 29—Inversion of the U wave during an attack of angina pectoris

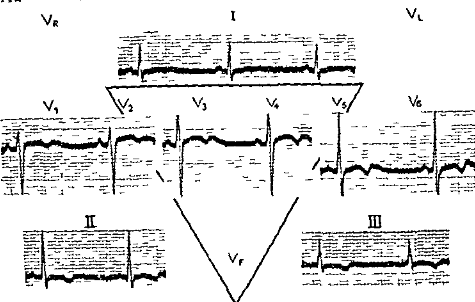



Fig 3 30—Carbon monoxide poisoning

normal level resulting in depression of the S T segment Impairment of coronary blood flow leading to anoxic injury is supposed to be maximal in the deeper layers of the myocardium because the intra myocardial pressure is highest in this situation so that there is no coronary flow during systole, near the surface coronary flow continues during systole and so insures a better supply of oxygen to the superficial myocardium

According to Prinzmetal (1954) however ischæmic depression of the S T segment is more likely to be due to functional changes in the outer layers of the myocardium

Permanent depression of the RS T segment in left ventricular surface leads or their equivalents may be seen in a minority of cases with severe ischæmic heart disease and in some cases of severe chronic anæmia In the latter the QRS voltage is usually lowered

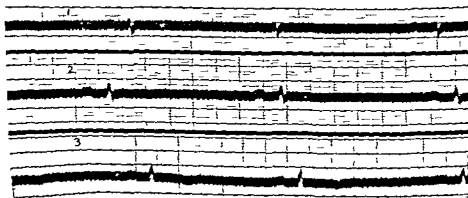



Fig 3 31—Myxœdema

*Myxœdema pattern* Flat or inverted T waves in all leads are characteristic of myxœdema (fig 3 31) In such cases the voltage of QRS is usually below 6 millimetres in the most favourable standard lead and there is often bradycardia Similar appearances may be found in chronic constrictive pericarditis in long standing cases of severe anæmia particularly pernicious and in anoxic chronic pulmonary heart disease but in these there is commonly tachycardia In severe cases of ischæmic heart disease with

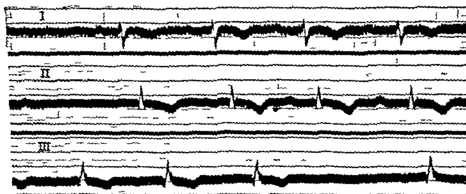



Fig 3 32—Pneumonic carditis There is partial heart block with dropped beats and inversion of the T wave in all leads

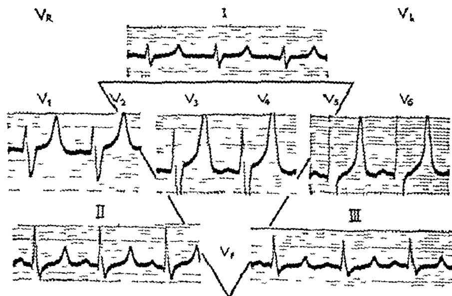



Fig 3 33—High voltage sharply peaked T waves in uræmia associated with a high blood potassium The long Q T interval is due to hypocalcæmia Widening of QRS due potassium is well seen in the chest leads

repeated myocardial infarction somewhat similar graphs may be encountered Indeed, when the whole heart is involved in any disease and when recurrent heart failure has occurred the voltage of QRS may be low and the T waves flat or slightly inverted in all leads, whatever the etiology

*Carditis pattern*

In any form of carditis but especially in diphtheria and least frequently in acute rheumatism, simple inversion of the T waves may occur and may favour any lead (fig 3 32) The RS T segment may be normal or depressed The voltage of QRS is usually normal

*Potassium T wave*

In uræmia when the blood potassium is high unusually sharp T waves of high voltage are often seen (fig 3 33) Similar T waves may be produced in normal subjects by raising the blood potassium to about 25 mg per cent by giving 10 to 20 G of potassium acetate by mouth * A high blood potassium also tends to rectify many forms of inverted T wave (fig 3 34) but not those due to myocardial infarction which may be exaggerated

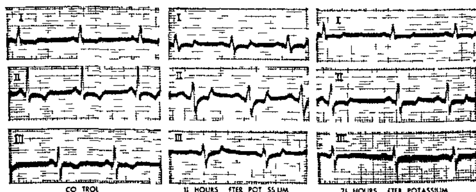



Fig 3 34—Effect of potassium on the T waves in a case of concordant left ventricular preponderance The QRS complex is also widened

(Sharpey Schafer 1943) Widening of P and QRS is also due to potassium and is seen in both illustrations

When the blood potassium is unduly low (<12 mg per cent) the S T segment and T wave may be depressed and the P R interval and Q $T_c$ prolonged (Perelson and Cosby 1949)

* This procedure is dangerous

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CHAPTER IV

# RADIOGRAPHIC DIAGNOSIS

## TECHNIQUE

THERE are at present six radiological methods applicable to cardiology fluoroscopy orthodiagraphy teleradiography kymography *tomography, and angiocardiography Fluoroscopy (screening)* is a routine diagnostic procedure orthodiagraphy is the construction of a simple tracing of the size and shape of the heart in any specified position as a supplement to fluoroscopy teleradiography is more accurate and should be preferred when facilities permit kymography records the character and amplitude of cardiac pulsation tomography is sectional radiography angiocardiography is the study of individual cardiac chambers or vessels with the aid of intravascular contrast media

### *FLUOROSCOPY*

With modern X ray equipment a remarkably clear view of the heart may be obtained The patient should be stripped to the waist and pressed close to the viewing screen The diaphragm which controls the diameter of the beam emitted from the X ray tube is first opened wide in order to view the thoracic contents as a whole In this preliminary survey attention is paid to the lungs to the costo phrenic angles and to the general size and shape of the heart The diaphragm is then constricted so that only the heart can be seen and the latter is observed more critically The size shape and pulsation of each part should be noted in regular sequence On the right side (fig 4 01) a faint slightly concave line, representing the superior vena cava descends from the sterno clavicular region close to the shadow of the vertebral column until it meets the ascending aorta which both displaces it to the right and causes it to become convex Below is the border of the right atrium which usually meets the diaphragm at a slightly acute

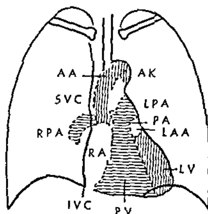



Fig 4 01—Diagram of postero anterior view of the heart as seen fluoroscopically

AA [illegible]
AK [illegible]
IVC [illegible]
LAA [illegible]
LV Left [illegible]
PA Pulm[illegible]ry art[illegible]ry
RA Right [illegible]
RV Right [illegible]
SVC [illegible]

angle The left border of the normal heart is made up of three convex curves from above downwards these are the aortic knob or knuckle the pulmonary arc, and the contour of the left ventricle Between the last two there is a small neutral segment or point of opposing movement which marks the left atrial appendage above it the pulmonary artery expands during systole while below the left ventricle contracts The hilar shadows are chiefly vascular the right pulmonary artery may be seen dividing early into upper and lower branches the former being indistinct the latter *sweeping* downwards in a well defined arc the left limb of the pulmonary artery forms the main pulmonary arc described above

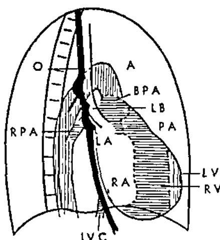



Fig 4 02 (a)—Diagram of right anterior oblique view of the heart as seen fluoroscopically (1st oblique position)

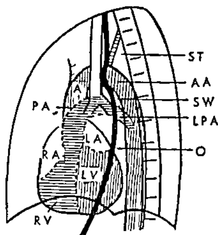



Fig 4 02 (b)—Diagram of left anterior oblique view of the heart as seen fluoroscopically (2nd oblique position)

| | |
|---|---|
| A | A rt c rch |
| B P A | B furc t on of th pulmo ry artery |
| I V C | I f io v n c |
| L A | L ft atr um |
| L B | L ft b on hus |
| P A | Pulmon ry ar |
| O | Bar um filled œsoph g |

| | |
|---|---|
| L P A | Left pulmo ry rt y |
| L V | L ft nt l |
| R A | R ght tr um |
| R P A | R ght pulmo ry t ry |
| R V | R ght v ntr l |
| S T | Sup o t t ngl |
| S W | S b ao t w ndow |

The patient is then turned into the first or right anterior oblique position The observer should place his gloved hands on the patient s hips and manually rotate him (so that the right shoulder is brought to the front) until the position is satisfactory The arms should be extended the left forwards and outwards the right backwards and outwards In this view (fig 4 02a) the ventricular shadows are superimposed and the right atrium is rotated towards the front so that little can be learned about these three chambers on the other hand the left atrium is outlined clearly as it forms the upper part of the posterior border of the heart Just anterior to the top of the left atrial curve a rather dense round shadow may be seen due to the bifurcation of the pulmonary artery it is connected with the anterior

ventricular border by a convex line representing the root of the pulmonary artery and conus of the right ventricle Above it are the superimposed shadows of the ascending and descending parts of the aortic arch If the patient is made to swallow a barium emulsion of the consistency of thick cream the œsophagus is outlined at the back of the heart under favourable conditions it is indented in turn by the arch of the aorta by the pulmonary artery and left bronchus and by the left atrium The left bronchus may be seen between the œsophagus and the rounded shadow of the dividing pul monary artery Between the œsophagus and the vertebral column there should be a translucent space

In the second or left anterior oblique position (fig 4 02b) the patient is turned to the right through an angle of about 45 degrees, the left shoulder being brought forwards In this view the two ventricles appear side by side the left forming the posterior border of the heart shadow and the right the anterior so that their contours can be readily compared The shadow of the right atrium overlaps that of the right ventricle the shadow of the left atrium lies posteriorly above the left ventricle Cranially the aorta and pulmonary artery may be seen as two arches one above the other separated by a light space known as the sub aortic window and crossed by the translucent trachea and left bronchus The aortic arch and descend ing aorta are well defined and shaped like an inverted J but the pulmonary artery is less distinct Above the aorta is another light space the supra aortic triangle bounded by the vertebral column posteriorly by the left subclavian artery anteriorly and by the aortic arch below The barium filled œsophagus is deflected to the patient s right as it crosses the aortic arch then lies in close relation to a short segment of the descending aorta leaves that vessel at about the level of the pulmonary artery and courses downwards and to the subject s right across the shadow of the left ventricle

*ORTHODIAGRAPHY*

Clips should be fitted to the viewing screen to enable tracing paper to be held firmly in position To make an accurate tracing of the heart shadow or orthodiagram special attention should be paid to five points First the position of the patient must be properly adjusted to the view required he must be pressed firmly against the screen and he should hold on to some support so that he can remain still Second the tracing should be made in mid inspiration and as it cannot be completed in one period of breath holding lines which move with respiration should be checked more than once Third to avoid distortion the cardiac outline must be traced by means of parallel rays this is accomplished by constricting the diaphragm to the smallest aperture consistent with adequate visualisation Fourth the greatest accuracy must be maintained when tracing the interior thoracic wall at its widest point and the lateral borders of the cardiac shadow so that the cardio thoracic ratio is reliable Fifth the finished

orthodiagram should be checked against the shadows traced to make sure the patient has not moved during the procedure

Fluoroscopes suitable for cardioscopy are so constructed that the X ray tube may be moved easily in any direction by the lever which operates the diaphragm In making the tracing the small light spot is run swiftly over the contours of the heart great vessels clavicles interior thoracic wall and diaphragm With experience it may be completed very quickly without danger of over exposing the patient or over heating the tube nevertheless a good technician switches off the current whenever momentarily dis engaged Fluoroscopy and orthodiagraphy are usually carried out with a power of 60 kilovolts and a current of 3 to 4 milliamps but with obese subjects it may be necessary to step up the kilovolts to 65 or 70 in order to obtain sufficient penetration Tracings are made with a wax pencil and it is helpful to add signs denoting the degree and direction of pulsation of important chambers and vessels

## *TELERADIOGRAPHY*

Skiagrams of the heart are always taken at a tube screen distance of at least 6 feet preferably 7 feet to avoid distortion by diverging rays The duration of exposure used to be half a second to ensure a diastolic record nowdays however it is commonly 0 1 second and this has introduced a source of error in interpreting serial skiagrams for one may be taken in systole another in diastole and the difference between the two may be appreciable The difficulty may be overcome by using a device whereby one of the electrocardiographic complexes such as R determines the moment of exposure Skiagrams of the oblique views are best taken when the most informative degree of rotation has been ascertained by previous fluoroscopy The normal appearances are illustrated in figure 4 03

## *KYMOGRAPHY*

A specially constructed kymograph may be attached to a teleradiograph for the purpose of recording cardiac pulsation (Stumpf 1931) A lead screen containing horizontal slits 11 mm apart is interposed between the film and the patient s chest and made to descend 1 cm during one com plete cardiac cycle The timing of the exposure is adjusted to synchronise with the descent of the grid In kymograms so obtained the lateral borders of the heart and great vessels appear toothed like the edge of a saw (fig 4 04) the ventricular crests representing diastole the troughs systole Pul sation is recorded in only one dimension i e in a plane parallel to the film but if the three standard views are photographed, the records are sufficiently comprehensive

The electrokymograph is a device for securing an accurate graphic record of pulsation at any point on the cardiac border (Henny and Boone 1947) A photosensitive pick up unit is placed between the patient and the screen so that the lead slit aperture lies across the border of the

heart at the point where it is desired to record pulsation The amount of light transmitted through the aperture varies with the movements of the cardiac border, and is recorded graphically by means of a galvanometer operated by the photo electric cell (fig 4 05) The interpretation of the graph is assisted by a simultaneous jugular phlebogram or electrocardio gram

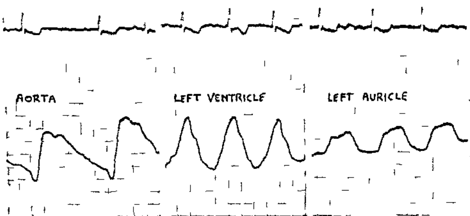



Fig 4 05—Electrokymogram from aorta left ventricle and left atrium in a case of mitral stenosis and incompetence with auricular fibrillation

Neither kymography nor electrokymography have fulfilled earlier expectations The former is too crude to be helpful and the latter too dependent upon the precise position of the slit in relation to the cardiac border being studied so that minor variations in the relationship may alter the graph profoundly

## *TOMOGRAPHY*

Body section radiography was introduced by Ziedses Des Plantes (1932) and others working independently to give radiological information about the lung and major bronchi when these were obscured by thoracoplasty pleural effusion or other large space filling lesion The technique was developed in Berlin by Chaoul and Grossmann (1935) and consists essentially of an arrangement whereby the X ray tube and film move through an arc in opposite directions during the period of exposure Only the plane focused is seen sharply structures anterior or posterior to it being blurred

Although tomography has been used very little in cardiology it may be helpful in demonstrating coarctation of the aorta (Twining 1937) calcified valves (Davies and Steiner 1949) metallic foreign bodies in the heart arteriovenous aneurysm of the lung and anomalous pulmonary veins It

is also helpful in distinguishing dilatation or aneurysm of the pulmonary artery or aorta from other mediastinal masses

Horizontal body section radiography has been used effectively by Stevenson (1950) to demonstrate a double aortic arch and other lesions or anomalies of the aorta

## ANGIOCARDIOGRAPHY

If a sufficient quantity of a radio opaque solution is introduced rapidly into the venous circulation its consecutive passage through the right heart pulmonary circulation left heart aorta and major arteries may be recorded by means of serial skiagrams (Castellanos *et al* 1938) The technique was elaborated by Robb and Steinberg (1938 1939) who used 20 to 60 ml of 70 per cent aqueous solution of diodrast A mechanical rapid casette changer enabled serial skiagrams to be taken at a rate of two per second (Sussman Steinberg and Grishman 1941) others preferred serial fluoro photographs obtained by means of a special camera or cinematograph (Stewart Breimer and Maier 1941)

At the time of writing the best contrast medium is a 70 per cent solution of diaginol the sodium salt of 3 acetylamino 2 4 6 triiodobenzoic acid which contains 66 per cent of iodine Patients are best lying down and should be given a preliminary dose of 1 ml to test for hypersensitivity if there is no urticarial reaction within half an hour serious hypersensitivity to iodine is unlikely Premedication varies in different clinics but a com bination of omnopon gr 1/6 to 1/3 or pethidine 50 to 100 mg and the



Fig 4 06—Normal angiocardiogram of right heart postero anterior view



Fig 4 07—Normal angiocardiogram of the right side of the heart second oblique position

anti histaminic phenergan 25 to 50 mg has proved satisfactory the latter is an additional sedative and combats both hypersensitivity reactions to iodine and vomiting from omnopon or pethidine Chlorpromazine is too strong a vasodilator An anæsthetic apparatus for delivering oxygen *under positive pressure* should always be available in cyanotic cases of congenital heart disease and adrenalin should be handy in cases of serious hypersensitivity



Fig 4 08—Angiocardiogram showing pulmonary veins and left atrium

A good cannula 6 to 9 inches long may be made from wide bore polythene tubing This is inserted into the antecubital vein and tied in position the proximal end being connected temporarily with a saline drip or simple syringe When all is ready 30 to 50 ml of diaginol warmed to blood heat is drawn into a strong 50 ml syringe and injected through *the cannula as rapidly as possible preferably in about two seconds*

Modern angriocardiographs are designed to take serial films at a rate of about four per second in postero anterior and lateral views simultaneously The right atrium is usually well filled 1 5 seconds after the start of the

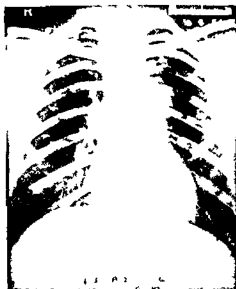


(a) Postero anterior



(b) Second oblique

Fig 4 09—Normal angiocardiograms of the left side of the heart



(a) Skiagram showing a mass between the aortic knuckle and the pulmonary artery

injection the right ventricle and pulmonary artery in 2 to 3 seconds the left atrium in about 5 seconds and the left ventricle and aorta in 6 to 9 seconds (figs 4 06 to 4 09)

The patient experiences a sensation of extreme heat but it passes rapidly The arrival of contrast medium in the lungs may excite a cough and nausea may follow The chief dangers however, apart from hypersensitivity to iodine are syncope due to a sharp fall in blood pressure resulting from general vasodilatation as recorded by Howarth (1950) sudden respiratory arrest and bronchospasm The combination of these adverse reactions may prove rapidly fatal in cyanotic cases of congenital heart disease for they may result in profound anoxia and secondary collapse of the basal centres Dangerous interference with the coronary circulation may also result from the sharp fall in blood pressure (Lawson 1945) The



Angiocardiogram showing normal pulmonary arteries distinct from the mass



(c) Angiocardiogram showing normal aorta d from the mass

Fig 4 10—Angiocardiographic proof that a mediastinal shadow was extra vascular

total mortality rate amongst 6 824 angiocardiographic examinations collected from the main investigatory clinics of the U S A Canada Great Britain and Sweden by Dotter and Jackson (1950) was 0 38 per cent The best treatment for acute pulmonary œdema due to iodine sensitivity is intravenous hydrocortisone

The amount of skin irradiation received by the patient during angio cardiography may be calculated when it is known that about 100 roentgen units are delivered by an X ray tube with the anode set at 90 cm from the skin and operating at 75 kV for 3000 mA second For example at this distance and power 100 r units would be delivered if the patient were exposed for 10 seconds at 300 mA Thus in angiocardiography if each film is exposed for 0 04 second and the tube is operated at 75 kV 450 mA and at a distance of 90 cm from the skin a series of 40 films would result in the patient receiving a skin dose of 25 r units When patients are screened X rayed frequently catheterised and angiocardiographed in two planes simultaneously considerable care must be taken to make sure they are not over exposed The maximum safe dose is 100 r in a week 200 r in a month and 300 r in a year but is *not repeatable*

Angiocardiography has proved especially helpful in establishing the diagnosis of congenital heart disease with right to left shunt e g Fallot s tetralogy pulmonary stenosis with reversed inter atrial shunt pulmonary hypertension with reversed shunt tricuspid atresia and transposition of the great vessels in demonstrating coarctation of the aorta in distinguish ing aneursym of the aorta or pulmonary artery from other mediastinal masses (fig 4 10) and pericardial effusion from cardiac dilatation and in showing the site of superior vena cava obstruction The subject has been well reviewed by Dotter and Steinberg (1951)

## SELECTIVE ANGIOCARDIOGRAPHY

Diaginol may be introduced directly into any part of the circulation that can be reached with a relatively wide bore catheter or needle As a rule complete angiocardiograms are more informative but under certain cir cumstances there may be great advantage in the selective technique for example if diaginol is introduced into the right ventricle and arrives immediately in the aorta it must have done so via a ventricular septal defect or because of transposition not via an atrial septal defect or foramen ovale

## RETROGRADE AORTOGRAPHY

Diaginol may also be introduced directly into the aorta via a catheter passed up the radial artery To overcome the resistance of the catheter which cannot be of very wide bore a special crusher has been designed by means of a long lever great force can be applied to the plunger of the syringe Retrograde aortography has been of value in demonstrating

coarctation of the aorta (fig 4 11) Good aortograms may be obtained in infants by forcibly injecting 5 ml of contrast medium into the brachial artery through a No 18 needle (Keith and Forsyth 1950) Diaginol may also be introduced into the aorta via a catheter inserted into the femoral artery or directly by needle puncture from behind (Dos Santos 1933 and 1937)



Fig 4 11—Retrograde aortogram showing coarctation of the aorta

Some risk is attached to these procedures Thus temporary hemiplegia has resulted when diodrast has been injected inadvertently into the common carotid artery (Peirce 1953) intermittent claudication in the hand and forearm has followed occlusion of the brachial artery and coronary occlusion is an obvious risk if a catheter is threaded too far down the ascending aorta Nevertheless relatively few complications have been reported and aortography may be helpful at times

## *CARDIAC MEASUREMENTS*

Numerous measurements have been elaborated to serve as indices of enlargement of the heart or of one or more of its chambers but they do not compare with expert opinion based on the methods already outlined The most reliable is the cardio thoracic ratio which is the transverse diameter of the heart (fig 4 12) over the widest internal diameter of the thorax and which should not exceed 0 5 In normal adults the transverse diameter of the heart averages 12 2 cm in the male and 11 cm in the female the range being 8 to 14 5 cm (Roesler 1937)

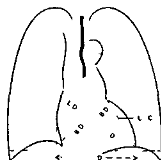



Fig 4 12—Diagram showing the common cardiac measurements

A Width of aorta
B D Broad diameter
L D Long diameter
L V C Left ventricular chord
T D Transverse diameter

The long diameter is measured from the junction of the superior vena cava and right atrium to the apex of the left ventricle and lies between 10 and 15 5 cm averaging 13 cm (Roesler 1937) It is especially increased in cases of left ventricular enlargement but it is also relatively increased in the long narrow heart of asthenic subjects

The broad diameter is the sum of two

perpendiculars drawn from the long diameter to the right cardio phrenic angle below, and to the point of opposing movement on the left border of the heart above and measures 7 to 11 cm in normal adults with an average of 9 cm (Roesler 1937) It may be increased in cases of mitral stenosis and pulmonary heart disease when the transverse and long diameters are normal

The location of the point of opposing movement is important for it tends to be raised or lowered according to whether enlargement is mainly left or right ventricular respectively Similar significance is attached to the length of the chord which subtends the arc of the left ventricle measured from the point of opposing movement to the left cardio phrenic angle this line is normally 6 to 12 5 cm long and averages 9 cm (Roesler 1937)

The antero posterior diameter of the heart is measured from teleradio grams taken in the lateral position and varies between 7 and 11 cm with an average of 9 cm It is a useful check on the significance of an increased transverse diameter for if this is due to cardiac enlargement the antero posterior diameter should be increased proportionately whereas if it is due to depression of the sternum the depth of the heart is decreased The antero posterior diameter is especially increased in mitral stenosis

The width of the aorta (2 to 3 cm) may be measured in the antero posterior or oblique positions whichever presents the clearest view of two sides of the vessel In the anterior view the measurement should be made from the left side of the barium filled œsophagus to the left border of the aortic knuckle but it is only valid when the posterior part of the aortic arch passes directly backwards i e in a direction perpendicular to the frontal plane In the oblique views barium in the œsophagus may also be helpful in the second oblique position for example the œsophagus may be deflected abruptly as it crosses the aorta so that the width of the vessel is seen clearly In practice a normal aorta is most easily measured in the postero anterior view a syphilitic atheromatous or unfolded aorta in the second oblique view

## NORMAL VARIATIONS

Both the size and shape of the heart vary greatly in normal individuals thus in children and adolescents the pulmonary artery may be relatively prominent (fig 4 13) in lean asthenic subjects the heart may be elongated and central in position (fig 4 14) in short stocky individuals it is apt to lie transversely (fig 4 15) rarely the left atrium can be seen in the P A view (fig 4 16)

Displacement or rotation of the heart to left or right is often due to scoliosis the common finding being displacement of the heart to the left the spinal curvature being convex to the right Rotation of the spine without conspicuous lateral curvature may cause considerable displacement or rotation of the heart When cardiac displacement is due to partial collapse



Fig 4 13—Teleradiogram [illegible] t [illegible] hild showing relative prominence [illegible] th pulmonary artery



Fig 4 14—The elongated centrally placed heart of a lean asthenic subject



Fig 4 15—Transversely placed heart of a short stocky subject



Fig 4 16—Skiagram of a normal heart in which the border of the left atrium is seen on the right side between the superior vena cava and the right atrium

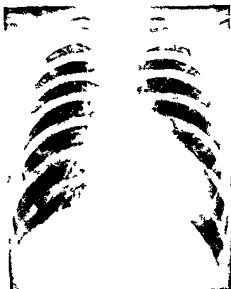


Fig 4 17—Displacement of the heart to the left without obvious cause



Fig 4 18—Displacement of the heart to the right attributed to old mediastinal pleurisy



Fig 4 19—Enlargement of the heart due to sinus brady cardia



Fig 4 20—Teleradiogram of an obese subject showing a triangular opacity at the apex of the heart (pericardial fat)



Fig 4 21—Apparent enlargement of the heart in a case of depressed sternum



(a) The heart in diastole



(b) The heart in systole

Fig 4 22—Teleradiograms of the same patient taken with short exposures showing difference in size of heart shadow in diastole and systole

of the lung increased translucency of the over expanded normal lung on the same side is usually observed and is a valuable sign when the collapsed part cannot be seen Occasionally the heart may be displaced to left or right without obvious cause (figs 4 17 and 4 18) Mediastinal pleural adhesions can be demonstrated in some of these cases (Kerley 1954)

Slight enlargement particularly of the left ventricle and of the transverse diameter is often seen in patients with slow heart rates whether due to sinus bradycardia, sino auricular block or to heart block The enlargement depends upon increased diastolic filling the slow rate being compensated by a large stroke volume (fig 4 19) Slight enlargement of similar type may be encountered in athletes in some it may be explained by sinus bradycardia which is common in these subjects but in others it may be due to the extra demands which have been made on the heart

In obese subjects the left cardio phrenic angle may be filled out by a triangular pad of fat (fig 4 20) this must not be confused with left ventricular enlargement In cases of depressed sternum the postero anterior skiagram may reveal general enlargement of the heart shadow but in the oblique views the depth of the heart is seen to be correspondingly reduced (fig 4 21)

When such causes can be excluded and unsuspected enlargement of the cardiac silhouette is revealed by a skiagram it is wise to check the technique employed Portable X rays or pictures taken with the patient lying or sitting may be misleading owing to distortion Short exposures may catch the heart in systole and a skiagram so obtained may be appreciably smaller than one photographed in diastole (fig 4 22)

The heart may be smaller than normal in many wasting diseases when atrophy takes place but this is of little practical importance

## RADIOGRAPHIC ABNORMALITIES

Some of the illustrations referable to this section may be found in other chapters but for the sake of convenience are reproduced here

### *ABNORMALITIES OF THE AORTA*

Saccular aneurysm (fig 4 23 a and b) is pathognomonic of syphilis It may be distinguished from other space filling lesions by its intimate connexion with the aorta in all views by calcification of its walls and by its pulsation a thrombosed sac however, may not pulsate Angiocardiography is helpful in doubtful cases Fusiform aneurysm (fig 4 24) usually means syphilitic aortic incompetence but may also be due to dissection and when confined to the ascending aorta to congenital hypoplasia both these conditions may also be complicated by aortic incompetence Fusiform aneurysm should be distinguished from prominence of the ascending aorta due to aortic stenosis or incompetence of any etiology (fig 4 25) Syphilitic aortitis without aneurysm or fusiform dilatation can only be diagno





(a) Anterior view (b) Second oblique position

Fig 4 23—Saccular aneurysm of the aorta

*(By  t y f S J h Park on)*





(a) Postero-anterior view (b) 2nd oblique position

Fig 4 24—Fusiform aneurysm of aorta

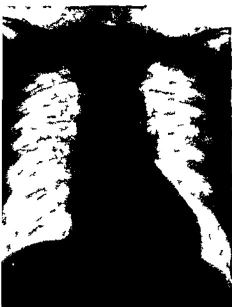


Fig 4 5—Prominence of the aorta due to rheumatic aortic incompetence



Fig 4 26—Unfolding of the aorta in hyper tensive heart disease



Fig 4 2 —Unfolding of the aortic arch illus trated by barium in the œsophagus

radiologically if inequalities of outline can be clearly demonstrated e g by means of angiocardiography

Unfolding of the aorta may occur in aortic valve disease in hypertensive heart disease and in atherosclerosis The ascending limb is conspicuous the knuckle is unduly prominent and the descending limb appears to the patient s left in the posterio anterior view (fig 4 26) In the second oblique position the arch is wider than normal and its posterior part may pull the œsophagus backwards (fig 4 27) Vigorous pulsation proclaims aortic incompetence rather than hypertension or atherosclerosis

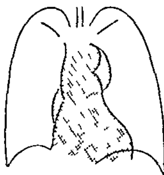


Fig 4 28 — Orthodiagram illustrating tortuosity of the *aorta*

Tortuosity of the aorta is characteristic of atherosclerosis it is best seen in the second oblique view but may be so marked that the descending limb appears to the right of the heart shadow in the postero anterior view (fig 4 28) Calcification of the aorta is of four main types (1) calcification of the ascending aorta is practically diagnostic of syphilis (2) a comma shaped calcified plaque in the aortic knuckle is characteristic of atherosclerosis (3) calcification outlining irregularities in the wall of the thoracic aorta in any position means syphilis (fig 4 29) (4) calcium is frequently laid down in the wall of a saccular aneurysm



Fig 4 29—Irregular calcification of the aortic arch in a case of syphilitic aortitis

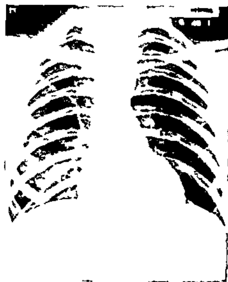


Fig 4 30—Coarctation of the aorta showing a prominent left subclavian artery elongated aortic knuckle post stenotic dilatation of a short segment of the descending aorta above the pulmonary arc rib notching and fullness of the left ventricle

Coarctation of the aorta may be recognised by the prominent left subclavian artery elongated aortic knuckle and post stenotic dilatation of a short segment of the descending aorta (fig 4 30) the diagnosis is confirmed by rib notching and enlargement of the left ventricle and denied by appearances indicating unfolding of the aorta

A right sided aortic arch is seen occasionally as an isolated congenital anomaly but more often it is associated with Fallot s tetralogy or Eisenmenger s complex The aortic knuckle projects to the patient s right and the barium filled œsophagus is deflected to the left (fig 4 31)

Hypoplasia of the aorta is rare as a solitary congenital abnormality but is common in association with certain other congenital or acquired lesions especially atrial septal defect and mitral stenosis The aortic knuckle is small and its pulsation diminished



(a) Anterior view



(b) First oblique position

Fig 4 31—Right s ded aortic arch illustrated by means of barium in the œsophagus
(By courtesy of J S J h Parkins )

## ABNORMALITIES OF THE LEFT VENTRICLE

Left ventricular enlargement is encountered chiefly in hypertensive heart disease aortic valve disease patent ductus arteriosus and organic mitral incompetence but may occur in various conditions as part of general enlargement It is easily recognised by the density and bulk of the left ventricular shadow in the postero anterior and second oblique positions by increase in the transverse and long diameters of the heart and th



Fig 4 32—Enlargement of the left ventricle due to aortic stenosis



Fig 4 33— Pulmonary venous congestion and bilateral hydrothorax from left ventricle failure

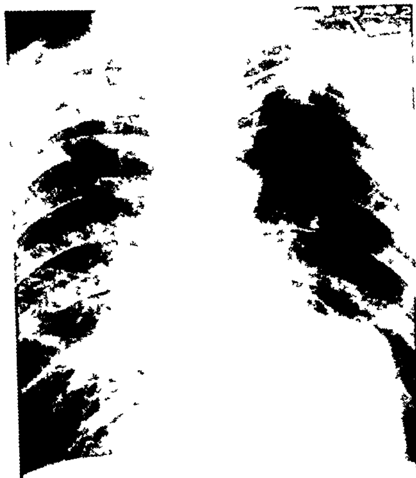


Fig 4 34—Left ventricular aneurysm



Fig 4 35—Calcified left ventricular aneurysm
(By the k[illegible] D[illegible] B H H[illegible])

left ventricular chord and by elevation of the point of opposing movement In hypertension and aortic valve disease the shadows of the unfolded aorta and of the heart itself may be compared either to two ovals set at right angles, or to the shape of a boot (fig 4 32)

When there is left ventricular failure (fig 4 33) the hilar shadows are exaggerated a fan shaped opacity appears at the hilum representing interstitial œdema and softer mottling spreads outward towards the periphery when there is pulmonary œdema Hydrothorax may be present and if unilateral is usually left sided (Bedford and Lovibond 1941)

Left ventricular aneurysm may present as a bulge on the left border of the heart usually towards the apex (fig 4 34) and may exhibit paradoxical pulsation occasionally the wall of the aneurysm is calcified (fig 4 35) Myocardial infarction may be located with precision in some cases by the fluoroscopic demonstration of an area with absent or paradoxical pulsation

## *DILATATION OF THE LEFT ATRIUM*

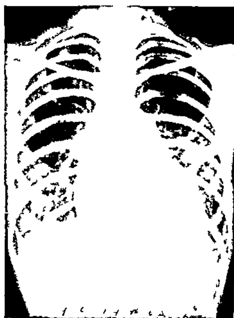
Conspicuous dilatation of the left atrium invariably means organic mitral valve disease but the chamber may be unduly full in cases of left ventricular failure In the postero anterior view it may appear as a bump on the left border of the heart between the pulmonary artery and left ventricle (fig 4 36) The proof that this bump represents the left atrium or left atrial appendage rather than the conus of the right ventricle is as follows (1) it is only seen in cases of mitral valve disease when it is related to the size of the left atrium not to the pulmonary vascular resistance (2) in angiocardiograms it opacifies with the left atrium not with the right ventricle (Grishman Sussman and Steinberg 1944) (3) it contracts with the atria in cases of complete heart block and expands with the rest of the left atrium in cases of severe mitral incompetence (4) it disappears after appendicular resection (fig 4 37) (5) if a catheter is introduced into the left atrium via an atrial septal defect or foramen ovale its tip can nearly always be passed to the very edge of the cardiac border at the site in question whereas in the conus of the right ventricle it is always well medial

On the right border of the heart an enlarged left atrium appears as a




Fig 4 36—Dilatation of the left atrium forming a bump between the pulmonary arc and left ventricle in a case of organic mitral incompetence





(a) (b)

Fig 4 37—Skiagram of a case of mitral stenosis showing (a) intense pulmonary venous congestion dilatation of the pulmonary artery and left atrium before operation and (b) disappearance of both the congestion and the left atrial appendage after mitral valvotomy and appendicular resection



Fig 4 38—Dilatation of the left atrium seen on both borders of the heart in the postero anterior view in a case of mitral incompetence



Fig 4 39—Dilatation of the left atrium illustrated by means of barium in the œsophagus Case of mitral stenosis Note the sharp curves produced by the aortic arch and the left bronchus and pulmonary artery




Fig. 4.40—Dilatation of the left atrium in a case of hypertensive heart disease (necropsy proof)

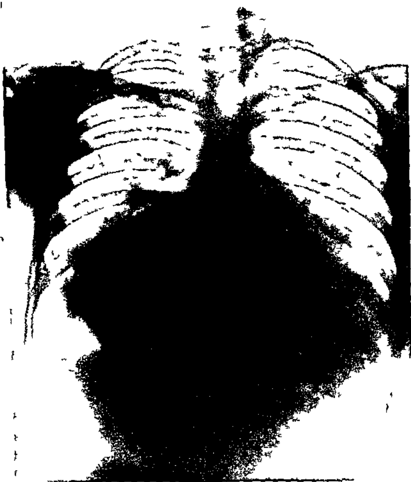


Fig 4 41—Aneurysmal dilatation of the left atrium in a case of mitral valve disease

convex shadow above but overlapping that of the right atrium (fig 4 38) The barium filled œsophagus is usually deflected to the patient s right in the postero anterior view

In the right anterior oblique position the œsophagus is displaced backwards in an abrupt manner immediately below the left bronchus and pulmonary artery (fig 4 39) the antero posterior diameter of the heart being increased and the retrocardiac space decreased correspondingly Backward displacement of the œsophagus from an enlarged left ventricle is rarely so abrupt or so high but on occasions it may be indistinguishable (fig 4 40) In the left anterior oblique position an enlarged left atrium causes the œsophagus to be deflected backwards above the shadow of the left ventricle

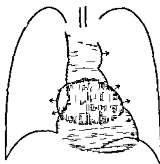


Fig 4 42—Orthodiagram illustrating expansile pulsation of the left atrium during ventricular systole in a case of organic mitral incompetence

Aneurysmal dilatation of the left atrium (fig 4 41) may be caused by rheumatic mitral incompetence or stenosis but it is probable that a high degree of atrial muscle damage is an important contributory factor

Systolic expansile pulsation of the left atrium is pathognomonic of mitral incompetence usually organic It is especially convincing when seen on both borders of the heart in the postero anterior view (fig 4 42) In the first oblique position backward pulsation of the left atrium is often seen in mitral stenosis but the quality and amplitude of the movement in organic mitral incompetence are most impressive and are easily recognised with experience

A rare complication of mitral stenosis is calcification of the left atrial endocardium

## *ABNORMALITIES OF THE PULMONARY ARTERY*

DILATATION OF THE PULMONARY ARTERY may be associated with congenital or acquired heart disease and is due to hypoplasia an increased pulmonary blood flow or pulmonary hypertension Congenital causes include idiopathic dilatation of the pulmonary artery pulmonary valve stenosis with normal aortic root patent ductus arteriosus ventricular septal defect atrial septal defect and Eisenmenger s syndrome acquired causes include primary pulmonary hypertension subacute thrombo embolic pulmonary hypertension hypertensive cor pulmonale pulmonary hypertensive mitral stenosis and other varieties of secondary pulmonary hypertension such as schistosomiasis periarteritis and disseminated lupus Slight dilatation of the pulmonary artery may occur in any of the hyperkinetic circulatory states and in passive pulmonary hypertension secondary to chronic left ventricular failure or mitral valve disease

In *idiopathic dilatation* the peripheral pulmonary vessels and the heart

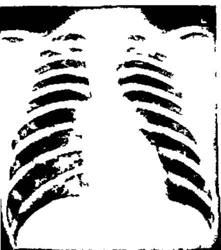


Fig 4 43—Idiopathic dilatation of the pulmonary artery

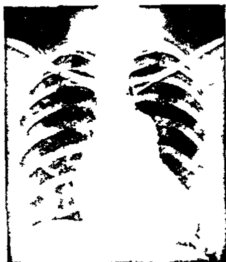


Fig 4.44—Dilatation of the pulmonary artery in a case of pure pulmonary stenosis



Fig 4.45—Dilatation of the pulmonary artery and its branches associated with left ventricular enlargement due to patent ductus

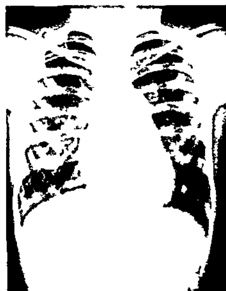


Fig 4.46—Dilatation of the pulmonary artery in a case of Eisenmenger's complex



Fig 4 47—Dilatat n of the pulm nary artery and its branches associated with hypoplasia of the rt and right d d enlargement in a case of atrial septal defect

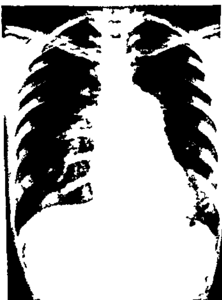


Fig 4 48—Dilatation of the pulmonary artery due to primary or idiopathic pulmonary hypertension



Fig 4 49—Dilatation of the pulmonary artery due to extreme pulmonary hypertension in a case of mitral stenosis



(a) Postero anterior view



(b) First oblique position

Fig 4 50—Dilatation of the pulmonary artery and its main branches in a case of chronic cor pulmonale due to emphysema

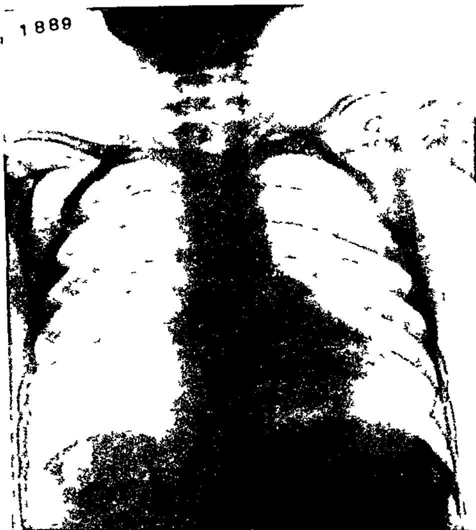



Fig 4 51—The Cœur en sabot due to Fallot s tetralogy

itself are normal (fig 4 43) unless there is secondary pulmonary incompetence when the right ventricle is dilated

In *pulmonary valve stenosis* (fig 4 44) the peripheral vascular markings may be diminished and the right ventricle and atrium enlarged according to the degree of stricture

In *patent ductus* dilatation of the pulmonary artery is due to an increased pulmonary blood flow and is associated with heavy pulmonary vascular markings and enlargement of the left ventricle (fig 4 45) the appearances in *ventricular septal defect* are similar except that the right ventricle is enlarged as well the appearances are also similar in *atrial septal defect* but here only the right ventricle and right atrium are enlarged (fig 4 47)

In *Eisenmenger s syndrome* dilatation of the pulmonary artery is due to pulmonary hypertension the peripheral vascular shadows are normal or light The right ventricle is hypertrophied but not dilated so that the transverse diameter of the heart may be normal (fig 4 46) as in Fallot s tetralogy

*Primary pulmonary hypertension* is characterised by dilatation of the pulmonary artery with diminished peripheral vascular markings due to pulmonary vasoconstriction and a low cardiac output (fig 4 48) The right ventricle and atrium are enlarged the left ventricle small Appearances are similar in subacute cor pulmonale from thrombo embolism

The degree of dilatation of the pulmonary artery in mitral stenosis is closely related to the pulmonary vascular resistance when this is extreme the radiological appearances may resemble those of primary pulmonary hypertension (fig 4 49)

In hypertensive cor pulmonale radiological evidence of emphysema polycystic lung or diffuse pulmonary fibrosis are added to the picture (fig 4 50)

HYPOPLASIA OF THE PULMONARY ARTERY is characteristic of Fallot s tetralogy (fig 4 51) There may be a distinct gap between the aortic knuckle and the curve of the left ventricle the vascular shadows at the hilum are reduced on both sides and the lung fields are remarkably clear

## *ENLARGEMENT OF THE RIGHT VENTRICLE*

Right ventricular enlargement is more difficult to recognise than left In the postero anterior view there is usually some increase in the transverse and broad diameters the right atrium being pushed a little to the right and the interventricular septum to the left

When hypertrophy of the right ventricle is associated with clockwise rotation of the heart the anterior edge of the septum forms most of the left border of the heart only the tip of the left ventricle being visible beyond it the effect produced is that of increased angularity of the cardiac apex and a more acute left cardiophrenic angle the general shape resembling the Dutch peasant s wooden shoe with turned up toe T



Fig 4 52—Right ventricular enlargement in a case of mitral stenosis (2nd oblique position)

is the cœur en sabot' and is especially characteristic of Fallot's tetralogy (fig 4 51)

When the right ventricle is dilated as well as hypertrophied as in atrial septal defect it may occupy the whole of the left border of the heart and form the apex beat proper in the postero anterior skiagram it is often impossible to be sure which ventricle is responsible for the enlargement and experience has proved over and over again that the electrocardiogram is a far more reliable guide

In the left anterior oblique position right ventricular enlargement is recognised by the increased curvature of the anterior border of the heart shadow Instead of the lob sided appearance resulting from normal left ventricular bias the heart shadow is more globular the anterior and posterior ventricular curves being more equal (fig 4 52) If the right atrium is enlarged however as may be determined from the postero anterior view interpretation is more difficult for its shadow is superimposed on that of the right ventricle in the second oblique position and it may be entirely responsible for the increased curvature of the anterior border

The right ventricle is enlarged particularly in pulmonary hypertension pulmonary stenosis pulmonary incompetence and atrial septal defect Hypertrophy rather than dilatation is characteristic of Fallot's tetralogy and Eisenmenger's complex dilatation usually means failure from pulmonary hypertension or simple pulmonary stenosis or an increased stroke volume as in atrial septal defect

## *ENLARGEMENT OF THE RIGHT ATRIUM*

Dilatation of the right atrium usually associated with fullness of the superior vena cava is seen in congestive heart failure atrial septal defect severe pulmonary hypertension or stenosis tricuspid stenosis or incompetence and Bernheim's syndrome

As a rule a dilated right atrium is recognised by its relatively low position on the right cardiac border and by the blunt angle it makes with the diaphragm (fig 4 53) When the left atrium appears on the right border of the heart it is higher more rounded, and forms a zone of



Fig 4 53—Gross enlargement of the right atrium due to tricuspid valve disease

## CONSTRICTIVE PERICARDITIS

The most important radiological evidence of constrictive pericarditis is loss of pulsation without cardiac enlargement but calcification of the pericardium is common and helpful and is usually best seen in the left anterior oblique position (fig 4 58) Slight to moderate enlargement of the heart shadow may occur if the pericardium is sufficiently thick (1 to 2 cm) but the triangular appearance given by the obliquely set straight right and left borders should suggest the correct diagnosis (fig 4 59)



4 58—Ca of chronic con tricti e peri itis sho ving extens e calcification of the pericardium (2nd oblique pos tion)

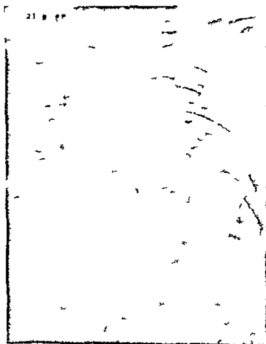


Fig 4 59—Chronic constrictive pericarditis showing triangular shaped heart in the anterior view

## CALCIFIED VALVES

Calcified valves are best seen fluoroscopically they may be recorded by means of tomography The patient should be turned 15 degrees to the left and an imaginary line drawn from the point of opposing movement on the left border of the heart downwards and to the patient s right at an angle of 45 degrees with the horizontal (fig 4 60) The aortic valve is situated just above this line in the centre of the heart shadow the mitral just below it and a little to the patient s left Calcification may be recognised by linear or anti clockwise elliptical movement of dense crescentic opacities in the direction of the anatomical axis of the heart synchronous with the heart

beat. The technique requires proper accommodation and maximum constriction of the diaphragm so that only a square inch or so of the screen is visible. Calcified aortic valves are sometimes better seen in the second oblique position where they lie at the intersection of a vertical line through

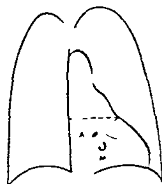



Fig. 4.60—Orthodiagram showing the position of calcified valves. The patient has been turned fifteen degrees to his left.

A. Aortic valve
M. Mitral valve

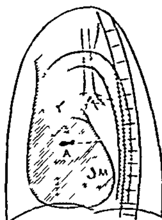



Fig. 4.61—Orthodiagram showing the position of calcified valves in the 2nd oblique position.

A. Aortic valve
M. Mitral valve

the centre of the heart shadow and a horizontal line through the top of the left ventricular arc (fig. 4.61). This view may be helpful in valve differentiation, for the mitral valve lies in the posterior third of the heart shadow and at a lower level (Sosman 1939).

## *PULMONARY VASCULAR SHADOWS*

Radiological examination of the heart is incomplete without careful inspection of the pulmonary vascular shadows. The normal lung markings are practically all vascular. The heavier shadows are arterial and taper evenly to the periphery.

In severe pulmonary hypertension due to a high pulmonary vascular resistance normal tapering disappears and is replaced by an abrupt change of calibre at a fairly proximal level: the main left and right pulmonary arteries are dense and dilated but the peripheral vessels are spidery and the outer lung fields unduly translucent (fig. 4.48).

*Pulmonary ischæmia* (or oligæmia) associated with a dilated pulmonary artery is characteristic of severe pulmonary valve stenosis, the diminished pulmonary blood flow being due to a low cardiac output or to reversed interatrial shunt (fig. 4.44).

Pulmonary ischæmia with a hypoplasic pulmonary artery is seen especially in Fallot's tetralogy (fig. 4.51) and tricuspid atresia.

Clear lung fields due to a diminished pulmonary blood flow are also seen in pericardial effusion Ebstein s disease (fig 4 62) and certain other low output states

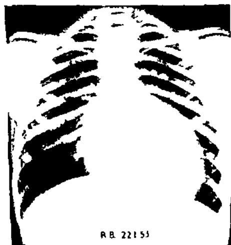



Fig 4 62—Pulmonary ischæmia associated with a low cardiac output in a case of Ebstein s disease the enlarged heart shadow is due to dilatation of the right ventricle and atrium

*Pulmonary plethora* may be defined as heavy pulmonary vascular markings due to an increased pulmonary blood flow the shadows are peripheral as well as central and are chiefly arterial Pulmonary plethora is seen in patent ductus arteriosus (fig 4 45) aorto pulmonary septal defect ventricular septal defect atrial septal defect (fig 4 46) anomalous pulmonary venous drainage transposition of the great vessels and persistent truncus arteriosus Heavy tapering vascular shadows spread far out into the lungs and in cross section form unusually dense round opacities

Other arterial abnormalities such as arterio venous fistula absence or occlusion of a major pulmonary artery and broncho pulmonary anastamoses are described elsewhere

*Pulmonary venous congestion* presents as fan shaped mottling spreading out from the hilum on each side (fig 4 37a) and is characteristic of mitral stenosis and left ventricular failure Heavy woolly shadows are superimposed in cases of pulmonary œdema Fine horizontal lines best seen near the right costophrenic angle represent engorged lymphatics (Kerley 1933)

Anomalous pulmonary venous drainage and anomalies of the venæ cavæ are described in Chapter VIII

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# SPECIAL INVESTIGATIONS

STETHOSCOPIC auscultation sphygmomanometry, ophthalmoscopy, electrocardiography and radiology have become routine technical methods of investigation which are used by the cardiologist before he arrives at his initial clinical diagnosis The techniques described in this chapter have not yet become routine in this country and are unlikely to do so for a precise etiological anatomical and functional diagnosis can usually be made without them and they infrequently reveal anything totally unexpected For the most part they are refinements of simpler techniques—accurate methods of measuring quantity when the quality of something is already known Occasionally they are used to solve a particular qualitative problem

## DIRECT MEASUREMENT OF THE VENOUS PRESSURE

Whilst elevation of the venous pressure is usually detected clinically with little difficulty there are occasions when it is valuable to check it by direct measurement (Moritz and Tabora 1910) The subject should be propped up at an angle of 30 to 45 degrees because patients with orthopnœa cannot lie flat and the technique should be the same for all cases The right arm bared to the shoulder is abducted to a right angle and supported on pillows so that the antecubital fossa is roughly at heart level An infusion needle connected to a spinal manometer or similar graduated glass tube is then inserted into the antecubital vein the zero mark on the manometer being placed at the level of the fourth costal cartilage by means of a spirit level the height to which blood rises above this mark represents the venous pressure Alternatively the zero mark may be placed at the level of the sternal angle or of some other reference point To avoid clotting a saline reservoir containing a drop of heparin should be attached to the system by means of a T shaped glass connexion as shown in figure 5 01 a few ml of the solution being

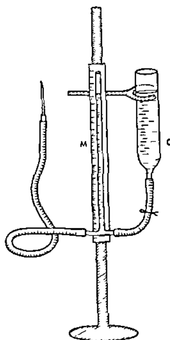



Fig 5 01—Apparatus for measuring the venous pressure
M Manometer graduated in cm
C Citrate or saline reservoir

allowed to flow through from time to time With this modification the manometer contains saline instead of blood The result should be expressed in cm of water (a horizontal line through the fourth costal cartilage with the patient at 45 degrees cuts the superior vena cava just above its junction with the right atrium) or in cm of water above or below the sternal angle If the technique is satisfactory the saline column should rise and fall gently with respiration and should rise sharply when the arm is constricted above the needle The normal venous pressure as so measured, ranges between 2 and 10 cm of water and averages 5 76 cm (Wood 1936) expressed with reference to the sternal angle it may be plus or minus 0 to 3 cm in relatively horizontal positions

In the *phlebomanometer* described by Burch (1950) a 12 cm glass observation tube with a bore of 1 00 mm is attached to the veni puncture needle and is connected by means of rubber tubing to the saline manometer through a three way tap which is also connected to a pneumatic pressure bulb Immediately before use 2 per cent sodium citrate is drawn up through the needle into the observation tube until the meniscus reaches a set mark When the needle is inserted into the vein the positive venous pressure tends to force the meniscus up the observation tube but this tendency is corrected by increasing the pressure in the pneumatic system connecting the tube with the saline manometer (by means of the pressure bulb) The pressure required to keep the meniscus at the mark is the venous pressure

## THE JUGULAR PHLEBOGRAM

*The polygraph* is an instrument for making simultaneous graphic records of two or more vascular pulsations Mackenzie (1902) concentrated on the jugular phlebogram as a means of analysing abnormalities of rhythm The instrument consists essentially of some sort of receiver which is placed over the internal jugular vein to pick up changes in volume or pressure connections to transmit these changes to the recorder an amplifying system to increase the magnitude of the changes and the recorder itself In Mackenzie s *clinical polygraph* which was made by Shaw the receiver was an open shallow cup and was connected pneumatically by means of a rubber tube to a tambour Amplification depended on the length of the lever (usually 6 inches) fixed to the membrane of the tambour The moving end of the lever was arranged to write on smoked paper covering a revolving drum Two or more such systems operated together so that the jugular pulse could be timed against the carotid or radial pulse and against the apex beat The disadvantages of this simple arrangement were the mechanical inertia of the levers the primitive method of recording and the pneumatic time lag

By cementing a small mirror to the membrane of the tambour in an eccentric position Frank (1903) overcame the problem of mechanical inertia *Optical records* were obtained by photographing the movements of

a beam of light reflected from the mirror the length of the beam providing excellent amplification But the *mirror capsule* was still operated by volume displacement in an air system and suffered from the same time lag as Mackenzie's instrument

To overcome this defect the receiver had to be some sort of transducer, i e a device which converts a pressure or volume change into a proportional electrical voltage A *carbon granule microphone* similar to that used in commercial telephony answers the purpose fairly well although it suffers from non linear distortion It consists of two electrodes between which are packed the carbon granules one of the electrodes is movable and is attached to a diaphragm which is displaced by changes in external pressure When the diaphragm is pushed inwards the carbon granules are compressed decreasing the resistance between the two electrodes A current flowing through the chamber is thus altered by any movement of the diaphragm The current can be led to a suitable galvanometer the movements of which can be recorded as in an electrocardiograph

*Piezo electric* (πιεζειν to press) *crystal microphones* have also been used with some success (Gomez and Langevin 1937 Miller and White 1941) They depend on the property of certain crystals such as quartz and Rochelle salt (sodium potassium tartrate) to develop electrical charges when subjected to mechanical strain The crystal must be cut in a special way, for it will only respond electrically when pressure is applied to it in a particular direction It is mounted between two electrodes one of them being fixed to a projecting button which can be placed on the jugular vein When the button is pushed in by the jugular pulse the crystal is compressed and electrical charges of equal amplitude and opposite sign proportionate to the stress develop on each side of the crystal these are picked up by the electrodes amplified and led to a suitable galvanometer and recorder

Microphone receivers are designed to be used in conjunction with multichannel recorders so that thermionic valve amplification galvanometer and recording device are already available The transducers themselves have a high frequency response linear in the case of the piezo electric type, and eliminate time lag Unfortunately the changes that develop are so small that no insulator is sufficiently perfect to preserve them for long so that these crystals cannot be used as transducers for electromanometers which are required to measure static and mean pressures

The *jugular phlebogram* is a good qualitative graphic record of what the clinician actually sees at the bedside it is not quantitative and cannot be standardised The venous pulse is said to travel at a rate of 1 to 3 metres per second (Morrow 1900) this means that the delay between right atrial and internal jugular events should lie between 0 15 and 0 05 sec which is rather longer than that found with modern techniques (about 0 05 sec in our own laboratories) In using the phlebogram to help identify phono cardiographic events this venous time lag must be borne in mind

The chief waves of the venous pulse have already been described in detail and are illustrated again in figure 5 02 The onset of *a* is 0 07 sec after the peak of the electrocardiographic P wave which signals the onset of right atrial contraction The prominent *c* wave is typical of jugular

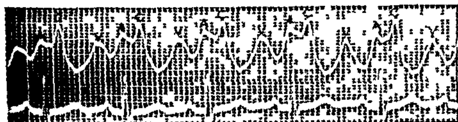


Fig 5 02—Jugular phlebogram

A Atrial contraction
C Carotid pulse
V The summit signals the opening of the tricuspid valve

phlebograms and is due to carotid pulsation The peak of *v* signals the opening of the tricuspid valve when allowance is made for time lag The two troughs are *x* and *y*

## THE ARTERIOGRAM

A *sphygmogram* (σφυγμος pulse) is a tracing or graphic record of any kind of pulse and although the original sphygmographs were designed for obtaining arterial pulse tracings and the word pulse customarily means an arterial pulse unless otherwise specified it is better to describe an arterial pulse record as an arteriogram and the procedure arteriography

Arteriograms may be recorded indirectly by placing a receiver over an arterial pulse or directly by inserting a needle into the artery *Indirect arterial sphygmographs* were in common use in the nineteenth century Marey (1863) designed and used an instrument which was of great help to Potain (1867) and in 1902 Mackenzie stated that the construction of these instruments was familiar to all medical men The receiver had a steel spring the foot of which was placed directly over the radial or other arterial *pulse a long lever was attached to the spring so that movements were* magnified and the lever was made to write on smoked paper The Dudgeon type was perhaps best known in this country Subsequent development has been the same as that described for jugular phlebographs and carbon microphones or piezo electric crystals electrical transmission thermionic valve amplification and electrocardiographic type of galvanometer and recording are now used

In the *direct method* a needle (18 to 20 gauge) is inserted into the brachial or femoral artery and is connected to a suitable manometer by a non elastic plastic or lead tube containing heparinised saline

*Manometers*

OPTICAL MANOMETERS use the principle of Frank s mirror capsule (q v ) In the instrument designed by Hamilton (1934) a 5 mm square 0 5 dioptre plano convex mirror silvered on the plane side was cemented eccentrically to a membrane made of brass 0 06 mm thick, or coin silver 0 0015 inches thick which formed the terminal face of a metal chamber fitted with citrate solution which was connected hydraulically by means of a lead tube to an 18 gauge Luer needle used for arterial puncture A slit lamp was arranged so that a beam of light up to 5 metres long was reflected from the mirror on to moving photographic film or paper The manometer could be standardised by recording the response to known changes of pressure the length of the beam of light being adjusted to the amplification required The response of the manometer was linear and of reasonably high frequency

This type of apparatus can also be used in conjunction with a *photo electric cell* which is influenced by the beam of light reflected from the mirror (Rein *et al* 1940) There are several kinds of photo electric cell, the principles of which may play an increasing part in medical recording devices In the *photo emission cell* a semi cylindrical silver cathode coated on the inside with a photo emitter (such as cæsium and cæsium oxide) faces an anode rod in a vacuum bulb When light falls on the photo sensitive surface of the cathode electrons are emitted in linear proportion to the quantity of light falling If a current is passed through the bulb it is increased by the additional number of electrons emitted by the light-sensitive cathode The variations in current so produced are directly proportional to the amount of light received and can be recorded by means of a galvanometer with suitable valve amplification

The *photo conductive* cell depends on the increased electrical conductivity of certain semi conductors such as selenium when exposed to light The response is again linear The cell is made in the form of a selenium coated grid through which a current can be passed The electrical resistance of the cell varies inversely with the amount of light to which it is exposed and this variation can be recorded in the usual way

The *photo voltaic cell* depends on the fact that an electromotive force is generated when light falls on the interface between a layer of copper and a layer of copper oxide or between layers of iron and iron selenide The layer of cuprous oxide or iron selenide must be very thin (less than 0 01 mm ) to allow the light to penetrate to the interface When the two layers are connected current flows in direct proportion to the quantity of light falling on the interface

ELECTROMANOMETERS transform pressures in the fluid system to equivalent electrical potentials directly and these are amplified sufficiently to operate suitable galvanometers A wide range of sensitivity allows pressure changes of 5 10 25 50 or 100 mm Hg to be represented by a deflection of 1 cm on the tracing *Transducers* for converting pressure changes into

equivalent variations in electrical potential are of various types according to the basic principle employed In practically all the fluid pressure acts on a membrane as with mechanical and optical manometers

*The strain gauge* makes use of the principle that wire increases its electrical resistance in proportion to the tension to which it is subjected Four strain sensitive wires are used and are attached to the membrane by cantilever suspension in such a way that movement in one direction increases the strain on one pair of wires and reduces it on the other movement in the reverse direction having the opposite effect When the membrane is at rest the resistances of the two pairs of wires are balanced on a Wheatstone bridge circuit When the resistances alter as a result of strain the bridge is thrown out of balance and current flows in the output or galvanometer circuit (Lambert and Wood 1947) If the bridge is powered by a 6 to 20 volt battery no amplification is necessary The frequency response is low at about 10 cycles per second The magnitude of the current is directly proportional to the movement of the membrane

*Inductance transducers* are based on Faraday's discovery in 1831 that an electrical current could be induced in a circuit by changing a magnetic field in the immediate vicinity of the circuit The induced current is increased if the coil is wound round a soft iron core If a battery current is flowing through the coil a magnetic field is set up around it which changes if the soft iron core is moved this change at once influences the current in the coil by setting up a secondary induced current Electromanometers have been designed in which the soft iron core of such a system is moved by a membrane influenced by changes of pressure (Wetterer 1944)

*Condenser or capacitance manometers* are based on the fact that if a condenser is incorporated in an alternating current circuit it acts like a resistance and since this resistance varies directly with the distance between the two plates the condenser can serve as a transducer if one of the plates is designed as a membrane which moves in response to changes of pressure Modern capacitance manometers are relatively complex (Hansen 1949)

*Clinical arteriogram*

Arteriograms are of limited clinical value because they reveal little that cannot be discerned with the trained finger A normal arteriogram (fig 5 01) usually exhibits two waves, P and D The former is the percussion wave and represents the rapidly transmitted shock of left ventricular contraction it is a pressure wave and must not be confused with blood flow Its velocity is 5 to 8 metres per second and is inversely proportional to the elasticity of the artery The length of the wave is 3 5 to 5 metres The time lag between aortic and carotid events is about 0 03 second and between carotid and radial 0 10 second (Lewis 1925) The sharp upstroke of a brachial arteriogram usually measures about 0 08 second and the rounded summit of the tracing occupies a similar period D is the dicrotic wave and

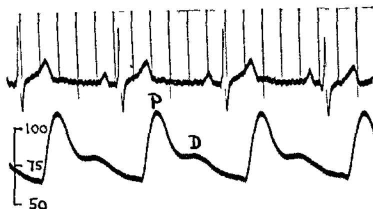



Fig 5 03—Normal arteriogram

is produced by the shock of aortic valve closure The latter synchronises with the *incisura (dicrotic or aortic notch)* which precedes the dicrotic wave Under certain circumstances e g in combined aortic stenosis and incompetence a second systolic wave T follows the percussion wave (fig 5 04)

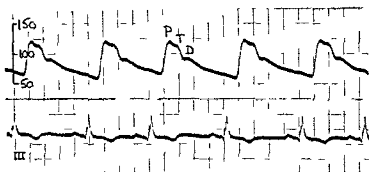



Fig 5 04—Direct arterial tracing showing a tidal wave T

Classical types of arteriogram have already been described in the clinical section on the pulse Direct arterial tracings are apt to be a little different and rather less like what one feels than the indirect The best example of this is the absence of a trough between percussion and tidal waves in the pulsus bisferiens in direct tracings (fig 2 04) The difference is attributed to the fact that a certain amount of external pressure is applied to the artery in indirect arteriograms just as it is when a clinician feels the pulse Direct tracings are similarly modified when external pressure is applied to the artery

The peak of the percussion wave of a direct arteriogram is the maximum systolic blood pressure the diastolic pressure is represented by the gentle

downward slope that succeeds the dicrotic wave The clinical diastolic pressure is the end of this slope i e the arterial pressure immediately preceding systole or the end diastolic pressure

A direct arteriogram may be recorded continuously over a long period if desirable e g when a continuous record of the blood pressure is required A special needle such as Riley s is then used and must be slipped well up the artery or a fine plastic catheter is threaded through the needle and the latter withdrawn Clotting may be prevented by including a slow high pressure saline drip in the system This does not influence the tracing

Arteriograms recorded simultaneously or consecutively with right ventricular pressures help to distinguish Fallot s tetralogy from pulmonary stenosis with normal aortic root in the former the systolic pressures are equal in the latter they are not The same principle serves to distinguish Eisenmenger s complex and pulmonary hypertension with reversed shunt through a patent ductus from other forms of pulmonary hypertension

Although the form of the arteriogram alone provides good evidence of the severity of aortic stenosis simultaneous brachial and left ventricular pressure tracings are better especially if the cardiac output at the time is known The left ventricular pressure is not easily measured but can be obtained by passing a fine nylon catheter through a needle inserted into the left atrium via the left bronchus or posterior chest wall (Bjork *et al* 1954) Direct puncture however is proving le s traumatic

Simultaneous or immediately consecutive direct arteriograms from the brachial and femoral arteries help to confirm or refute the presence of coarctation of the aorta when the diagnosis is in doubt In coarctation the femoral arteriogram shows a lower systolic pressure and a smaller pulse pressure than the brachial while the percussion wave is more prolonged and has a delayed summit

Continuous arteriograms have also proved helpful in the investigation of syncope and in studying the effects of the Valsalva manœuvre

*The Valsalva manœuvre*

The Valsalva manœuvre consists of forced expiration against a closed glottis (Valsalva 1707 Dawson 1943) It is a simple way of greatly raising the intrathoracic pressure The effect is more conveniently achieved by blowing up a column of mercury and maintaining the pressure at 50 mm Hg or as near to this level as possible This is then the intra oral pressure and may be assumed to be also the intrabronchial and intrapleural pressure Alternatively the intrathoracic pressure may be measured by passing a thin water filled polythene tube down the œsophagus (Dornhorst and Leathart 1952) the tube has an internal diameter of 0 5 mm and should have two or three lateral holes cut near the distal end The obstruction at the thoracic inlet tends to prevent cardiac filling and the heart

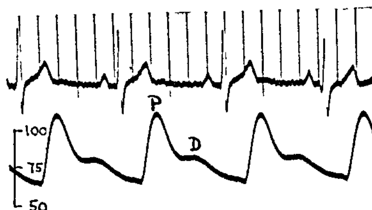



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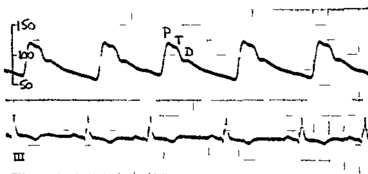



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The peak of the percussion wave of a direct arteriogram is the maximum systolic blood pressure the diastolic pressure is represented by the gentle

## THE CIRCULATION TIME

The circulation time may be measured from the antecubital fossa to the head and neck via the heart and lungs (Blumgart 1931) Numerous substances may be used for the purpose and fall chiefly into four groups illustrated by sodium cyanide histamine sodium dehydrocholate and fluorescein

If 0 25 to 0 5 ml of 2 per cent *sodium cyanide* is injected into the antecubital vein the patient takes a sudden deep breath when the substance reaches the carotid sinus the respiratory reflex being initiated by direct chemical action (Robb and Weiss 1934) At the same time the sinus node is depressed so that the objective end point is also signalled by a sinus pause which can be recorded and timed exactly on the electrocardiogram (Wexler *et al* 1947) Sodium cyanide is rapidly rendered inert by oxidation so that the test may be repeated almost immediately if necessary Unfortunately patients vary considerably in their susceptibility to the drug and as this cannot be predicted the minimum dose must be tried first the sensation of choking and strangling which may follow too large a dose in sensitive individuals may be very unpleasant *Lobeline* in doses of 2 5 to 5 mg acts similarly on carotid chemoreceptors and any record of respiration will signal the end point objectively It is safer and less unpleasant than cyanide (Berliner 1940)

*Histamine phosphate* (Weiss Robb and Blumgart 1928) in doses of 0 001 mg per kg of body weight in 1 5 000 solution induces a sudden facial flush when it reaches the capillaries of the head and neck It is not recommended owing to the uncertain end point and subsequent headache recorded times are too long

A 20 per cent solution of *sodium dehydrocholate* (decholin suprachol) has been used extensively and has given satisfactory results but sometimes causes vomiting (Winternitz *et al* 1931) A dose of 3 to 5 ml is injected rapidly through a wide bore needle the patient having been warned to raise the other hand smartly the instant he should notice a strange taste in or under the tongue This taste is peculiarly intense and bitter so that it is difficult for the patient to be mistaken about the moment of its arrival and objective confirmation may be obtained by the involuntary grimace that accompanies it The time should be measured from the beginning of the injection to the end point described A concentrated solution of *saccharin* (2 5 G in 4 ml of water) which produces a sweet taste when it reaches the tongue is less unpleasant does not cause vomiting and may be repeated if serial observations are required (Fishberg Hitzig and King 1933) but it is apt to cause local venous thrombosis *Calcium gluconate* 2 5 to 5 ml of a 20 per cent solution causes a hot sensation in the back of the tongue and throat (Goldberg 1936) and *magnesium sulphate* 6 ml of a 10 per cent aqueous solution has a similar end point (Neurath 1937 Bernstein and Simkins 1939) these substances may be alternated with advantage if test is repeated for they are physiological antidotes In this group

end points are all subjective but should not be despised on that account for they are usually sharp and clear

The fourth class comprises substances that give an objective end point wherever desired In their original papers Blumgart and Weiss (1927) used *radium C* and a special detector which operating at any given point in the circulation would signal the arrival of the test dose The same principle has been employed by Prinzmetal (1948) using *radiosodium* ($Na^{24}$) and a Geiger-Muller counter for constructing time concentration curves of the test dose as it passes through the right and left side of the heart If within a minute of raising a histamine wheal (using 0 1 ml of a mixture of equal parts of 1 1 000 histamine phosphate and 2 per cent procaine) on any part of the skin a fluorescent substance is injected intravenously fluorescence develops at the periphery of the wheal as soon as the substance reaches it a suitable ultraviolet lamp is required The best substances for this test are *fluorescein* (Lian and Barras 1950) and *riboflavine* the dose of the former being 5 4 mg per kilogram of body weight and of the latter 0 8 mg per kilogram (Winsor *et al* 1947)

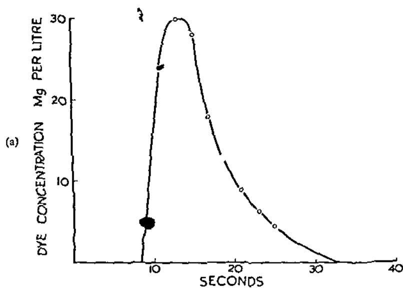
The *normal arm to tongue circulation time* averages 13 5 seconds with extremes of 9 to 18 seconds (Wood 1936) *The time is fast* (6 to 9 sec ) in all the hyperkinetic circulatory states and may be very fast (3 to 5 sec ) in congenital heart disease with large right to left shunt *The time is greatly prolonged* in cases of left ventricular failure when it averages 28 seconds it is variable in mitral stenosis according to the physiological situation and only slightly prolonged if at all in pure right ventricular failure The circulation time is also related to the size of the heart particularly to the residual stroke volume (Gernandt and Nylin 1946) and is prolonged in myxœdema

The *arm to-lung time* may be measured by injecting 0 25 ml of ether into the antecubital vein its arrival in the capillaries of the lung being signalled by a sudden cough or deep dreath and by the smell of ether in the expired air Amyl acetate may also be used the smell of pear drops being un mistakable when it reaches the lungs The normal time averages 6 seconds and ranges between 3 5 and 8 seconds (Hitzig 1935) The test has limited value as explained on page 278

## DYE DILUTION CURVES

The injection method of measuring the cardiac output (Stewart 1897) was taken up in 1929 by Kinsman Moore and Hamilton who studied the behaviour of a small quantity of dye when injected rapidly into models of the circulation The dye diffused uniformly in the turbulent stream and moved forwards in an ever widening band If samples of the fluid stream were taken at frequent intervals from a point well away from the site of injection and the quantity of dye in each sample measured colorimetrically against known standards a curve could be constructed in which the concentration of dye in mg per litre was plotted against the time (in

(a)




(b)

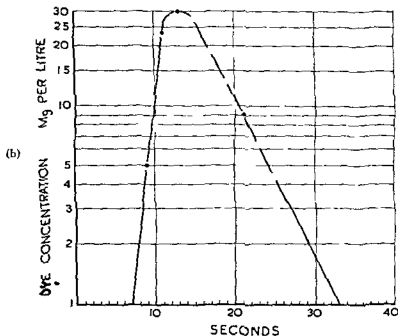



Fig 5 06—Time concentration curves
(a) Plotted in a l near manner on both s ales
(b) Concentration plotted logarithmically (see text)

seconds) at which the sample was obtained after the onset of the injection Such time concentration curves had a characteristic shape as shown in figure 5 06a The build up of concentration second by second was rapid the disappearance of dye more gradual and fading off towards infinity If recirculation was arranged to make the model more realistic the downstroke of the curve was interrupted by a sudden increase of concentration as the dye entered its second circuit This made it impossible to estimate the time at which the dye would have disappeared from samples had it not recirculated The difficulty was overcome when it was recognised that the down stroke of the curve had a logarithmic shape and when the concentration of dye was plotted logarithmically the time scale remaining linear the downstroke became a straight line (fig 5 06b) By extending the top part of the slope until it met the time scale it was then possible to tell when the dye would have disappeared had it not recirculated

Suppose now the duration of such a time concentration curve is 30 seconds and the mean concentration of dye over that period is 10 mg per litre then if the amount of dye injected was 20 mg it is clear that this must have been diluted by 2 litres of blood in 30 seconds i e by a blood flow or cardiac output of 4 litres per minute

$$\text{Thus F or C O} = \frac{I \times 60}{ct}$$

where F is the blood flow in litres per minute
I is the quantity of dye injected in mg
c is the mean concentration of dye in mg per litre
t is the duration of the time concentration curve in seconds

The mean concentration of dye is the average of all the samples taken second by second over the period of the time concentration curve In the hypothetical curve plotted in fig 5 06 the mean concentration of dye works out at 12 mg per litre over a period of 24 seconds Had 24 mg of dye been injected the cardiac output per minute would have been $\frac{24 \times 60}{12 \times 24} = 5$ litres

When compared with the Fick principle for measuring cardiac output in animals results obtained by the dye injection method tallied remarkably closely the average difference between the two being only 0 2 per cent (Moore *et al* 1929) Nearly twenty years later Hamilton and his colleagues (1948) compared the two methods in man and again average results were almost identical

The dye commonly used now is Evans blue in a dose of 10 to 20 mg (2 to 4 ml of a 0 5 per cent solution) An ear oximeter of the photo electric cell type designed by Millikan (1942) and modified by Wood and Geraci (1949) may be used instead of direct arterial sampling at two second intervals Time concentration curves can be recorded directly by means of a galvanometer with this oximeter (Beard and Wood 1951)

Dye dilution curves may also be used in the study of intracardiac shunts

and other cardiovascular abnormalities (Nicholson Burchell and Wood 1951) With left to right shunts as in atrial septal defect ventricular septal defect and patent ductus the initial part of the curve is more or less normal in that dye arrives at the ear in normal time builds up quickly and starts disappearing quickly although its mean concentration is diminished but recirculation occurs early and may be repeated once or twice producing a series of irregular bumps during the return of the graph to normal With right to left shunts as in Fallot s tetralogy dye arrives at the ear well ahead of normal time giving rise to a premature hump on the upstroke of the normal curve (Swan *et al*, 1953)

*Pulmonary blood volume*

Dye dilution curves offer an objective method of measuring the mean pulmonary circulation time (Hamilton *et al* 1932), and since the cardiac output at the time can be estimated by the same technique the amount of blood in the lungs can be calculated from Stewart s formula which states that

$$Q = \frac{VT}{60} \text{ (Stewart 1921)}$$

where Q is the quantity of blood in the lungs in litres
V is the pulmonary blood flow in litres per minute and
T is the mean pulmonary circulation time in seconds

In the hypothetical example illustrated in figure 5 06

$$Q = \frac{5 \times 12 \text{ (say)}}{60} = 1 \text{ litre}$$

When measuring the pulmonary circulation time by means of radium C Blumgart and Weiss (1928) calculated that the average quantity of blood in the lungs of normal subjects was 984 ml or 21 per cent of the total blood volume

*Total blood volume*

The circulating blood volume is normally around 5 to 6 litres it is about 3 to 3 5 litres per square metre of body surface or about 75 to 85 ml per kilogram of body weight and averages a little more in men than in women owing to a rather higher red cell content in men Plasma constitutes about 55 per cent and cells about 45 per cent of the volume of whole blood

It may be estimated by injecting intravenously a known quantity of a substance with suitable characteristics and measuring its concentration in the blood after complete mixing has occurred Evans blue dye (Gregersen *et al* 1935) has proved satisfactory and may be given in a dose of 5 ml of a 0 5 per cent solution its concentration in the plasma being determined colorimetrically The dye technique originally introduced by Keith Rowntree and Geraghty in 1915 has largely replaced the older carbon monoxide method of Haldane and Smith (1900) in which a known quant

of the gas was inhaled and its concentration in the blood measured by means of a colorimeter or by blood gas analysis The injection of radio active substances such as tagged red cells is now challenging the dye method or is being employed as a supplement to it for tagged red cells are used for measuring the total circulating red cell volume whereas dyes measure plasma volume Of course the relative quantities of red cells and plasma in whole blood can be determined easily by the hæmatocrit

## CARDIAC CATHETERISATION

Although first performed by Forssmann (1929) on himself the introduction of cardiac catheterisation as an aid to clinical diagnosis is largely due to the work of Cournand (1941) in the U S A and of McMichael and Sharpey Schafer (1944) in England

*Cardiac output*

Up till then measurement of cardiac output in man depended on methods which could not directly utilise the important principle first enunciated by Fick (1870)

$$\text{C O (L/min)} = \frac{\text{oxygen consumption (ml min)}}{\text{A–V oxygen difference (ml/L)}}$$

For example, if an individual extracts 250 ml of oxygen from the atmosphere per minute and the difference in oxygen content between samples of blood from the pulmonary artery and samples from the pulmonary veins (arterio venous oxygen difference) is 50 ml per litre then clearly 5 litres of blood must have passed through the lungs per minute It was easy enough to measure the oxygen consumption and the oxygen content of arterial samples but short of direct puncture there was no means of obtaining a mixed venous sample from the right side of the heart Cardiac catheterisation however at once made this possible and since its introduction a vast amount of accurate work on the cardiac output in health and disease has been carried out

*Pressures in the lesser circulation*

At the same time cardiac catheterisation supplied another great need for it offered a direct and relatively safe method of measuring *pressures in the right side of the heart* and pulmonary artery—a previously inaccessible part of the circulation Hamilton s optical manometer already in use for measuring arterial pressure (q v ) allowed systolic and diastolic pressure to be measured accurately and soon a number of electromanometers were adapted or designed for the same purpose

It was discovered later that if the catheter was passed down a branch of the pulmonary artery as far as it would go the tip usually became wedged in such a manner that a little force was required to withdraw it The pressure recorded when the catheter was so wedged was called the *pulmonary capillary venous pressure* for it was believed to represent just that

(Hellems *et al* 1948 Lagerlof and Werko 1949) Samples withdrawn from such a site are always near 100 per cent oxygenated and must not be used as an indication of the oxygen saturation of pulmonary venous blood In fact however the pressure obtained when a catheter is wedged in a pulmonary artery branch is the left atrial pressure (fig 5 07) and the wave

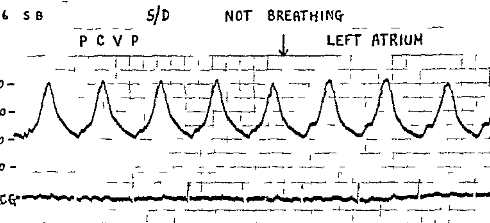



Fig 5 07—Immediately consecutive tracings from a wedged pulmonary artery and from the left atrium (via the left bronchus) in a case of mitral incompetence showing an identical pressure pulse in the two situations (from the paper by Epps and Adler from the Cardiac Department of the Brompton Hospital)

form is identical with the left atrial pressure pulse (Epps and Adler 1953)

If the left atrial pressure pulse cannot be obtained indirectly in this way it can be recorded directly by inserting a needle into the left atrium via the left bronchus (Facquet Lemoin *et al* 195-) or by paravertebral puncture (Bjork *et al* 1953) Even left ventricular pressures can be recorded via similar routes (Bjork *et al* 1954)

*The pulmonary vascular resistance* can be calculated when the cardiac output mean pulmonary artery pressure and mean left atrial pressure are known according to Poiseuille s equation

$$\text{Resistance (R)} = \frac{\text{pressure gradient}}{\text{flow}}$$

which adapted becomes

$$R = \frac{\text{P A P} - \text{L A P (mm Hg)}}{\text{pulmonary blood flow (L/min)}}$$

The result may be expressed in simple units of resistance If it is desired to express resistance in fundamental units of force as described by Gorlin and Gorlin (1951) pressures in mm Hg must be converted into

dynes/cm and flows expressed in litres per minute must be converted in cm ³/sec The equation thus becomes

$$R = U \times \frac{0\ 1 \times 13\ 59 \times 981\ 17\ \text{dynes/cm}}{1\ 000\ \text{cm}^3/60\ \text{sec}}$$

where U stands for the simple unit already described The figure 13 59 is the specific gravity of mercury and 981 17 cm per second per second is the g factor—that is the acceleration force of gravity The dividend thus becomes 1 333 4 dynes/cm The equation may now be rewritten

$$R = U \times \frac{1\ 333\ 4\ \text{dynes} \times 60\ \text{sec}}{1\ 000\ \text{cm}^5}$$

$$= U \times 80\ 004\ \text{dynes sec /cm}^5$$

Thus it is only necessary to multiply the unit by 80 to express the resistance in dynes sec /cm ⁵

*Shunts*

As cardiac surgery advanced accurate methods of diagnosing the various forms of congenital heart disease became imperative and in this new field cardiac catheterisation helped enormously In left to right shunts samples from chambers beyond and including that which receives the shunt contain more oxygen than samples taken from chambers proximal to the shunt For example in ventricular septal defect samples from the venæ cavæ and right atrium may be 70 per cent saturated with oxygen when samples from the right ventricle and pulmonary artery are 80 per cent saturated proving that arterialised blood has entered the right ventricle from the left side of the heart Since the pulmonary blood flow and the systemic blood flow can be measured separately, the size of the shunt can be calculated

$$\text{Pulmonary flow (L/min)} = \frac{\text{oxygen consumption (ml /min )}}{\text{P V} - \text{P A oxygen content (ml /L )}}$$

$$= (\text{say}) \frac{240}{190 - 160} = 8\ \text{L /min}$$

$$\text{Systemic flow (L/min)} = \frac{\text{oxygen consumption (ml /min )}}{\text{Art} - \text{R A oxygen content (ml /L )}}$$

$$= \frac{240}{190 - 140} = 4\ 8\ \text{L /min}$$

Thus in this example the interventricular shunt is 3 2 L /min Pulmonary venous blood can only be obtained if the catheter passes through a foramen ovale but for practical purposes may be assumed to be the same as arterial blood provided there is no right to left shunt

In cases of right to left shunt samples from all chambers in the right side

of the heart are similar but the arterial oxygen saturation is reduced In such cases

$$\text{Pulmonary flow} = \frac{\text{oxygen consumption}}{\text{P V} - \text{P A oxygen content}}$$

$$= (\text{say}) \frac{210}{190-120} = 3 \text{ I /min}$$

$$\text{Systemic flow} = \frac{\text{oxygen consumption}}{\text{arterial} - \text{R A oxygen content}}$$

$$= (\text{say}) \frac{210}{160-120} = 5\ 2 \text{ L /min}$$

giving in this instance a right to left shunt of 2 2 I /min In making the calculation it has been assumed that the pulmonary venous blood is 95 per cent saturated i e having an oxygen content of 190 ml /L (oxygen capacity with normal hæmoglobin 200 ml /L ) It should perhaps be explained that in calculating the systemic blood flow the arterial oxygen content from which the arterio venous oxygen difference is partly derived is made up of two components the content of blood which has passed through the lungs and picked up all the oxygen consumed and the content of the shunted blood which has picked up no oxygen at all It is as if the full 5 2 litres passed through the lungs but 2 2 of them failed to pick up any oxygen

Further information in congenital heart disease may be obtained if the catheter passes through a septal defect into the left side of the heart or into anomalous veins

## *TECHNIQUE*

Radio opaque nylon catheters 100 to 125 cm long are made in seven sizes (nos 4 to 10) the smallest (no 4) having an internal diameter of 0 5 mm and an external diameter of about 1 3 mm and the largest (no 10) having an internal diameter of about 1 8 mm and an external diameter of 3 2 mm when filled they contain from 0 3 to 3 9 ml of saline the common sizes (nos 6 7 and 8) containing 0 8 1 2 and 1 5 ml respectively They are sufficiently pliable to loop easily inside the heart or blood vessels yet not so soft as to lose their elasticity as soon as they are warmed in the blood stream The distal end is bent at about 4 cm from the tip so that awkward angles can be negotiated After use the catheters are washed out with tap water and then with a hydrogen peroxide drip for several hours to remove any particles of blood enmeshed in the weave with which the catheters are lined if this is neglected rigors may arise from pyrogens washed out of the lining of the catheter when it is next used and can be very dangerous in certain types of heart disease The catheters are then sterilised in hot formalin vapour and may also be stored in formalin vapour They should not be boiled or autoclaved

The patient is prepared with omnopon gr 1/6 to 1/4 or pethidine 50 to 100 mg and phenergan 25 mg The latter acts as an additional sedative and tends to prevent vomiting Pentothal may be necessary in children under six Neither quinidine nor procaine amide are now given as a routine beforehand because they did not prevent or diminish the frequency of ectopic beats or other changes of rhythm and they are undesirable for three other reasons (1) they may diminish the peripheral resistance (2) they encourage cardiac standstill in the rare event of transient heart block during catheterisation (3) they may turn pre existing or a paroxysm of atrial fibrillation into flutter with a faster ventricular rate Procaine amide, however is always kept handy so that 0 5 to 1 G may be given through the catheter immediately in the event of paroxysmal ventricular tachycardia or fibrillation Noradrenalin 100 μg in 10 ml of sterile water is also kept ready in a second syringe in hazardous cases for restoration of normal rhythm by means of heavy doses of procaine amide may not restore the blood pressure Penicillin, 1 million units is given as a routine to help prevent infection

The patient is laid flat on a foam rubber mattress overlying an X ray couch a window is cut out of the mattress to facilitate fluoroscopy The couch should be constructed so that it can be tilted easily and should be freely accessible from either side

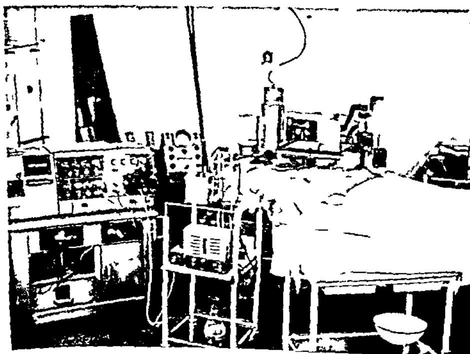


Fig 5 08—Photograph of the N E P multichannelled recorder Sanborn *electromanometer* and cathode ray monitor used for cardiac catheterisation at the Institute of Cardiology

The right median cubital vein or the right basilic vein below or above its junction with the cubital vein is exposed after liberal dermal anæsthesia with 1 per cent procaine *The right arm is preferred because* the catheter is easier to manipulate from this side (especially if the operator is right handed) because the route is a little shorter (important in large adults if an indirect left atrial pressure tracing is required) and to avoid a left sided superior vena cava entering the right atrium via the coronary sinus a very difficult route from which to catheterise the pulmonary artery (encountered in 6 per cent of cases especially in Fallot s tetralogy) *The median vein* is always chosen because it offers no obstruction to the passage of a catheter whereas the cephalic route proved impossible in 19 out of 30 cases in which it was tried *Liberal dermal anæsthesia* means raising an extensive wheal in the skin overlying the vein using about 10 ml of 1 per cent procaine subcutaneous anæsthesia wears off too quickly and stronger solutions of procaine are initially more painful and may upset previously good sedation in a small child Efficient dermal anæsthesia has made venospasm very rare

A catheter should be chosen which fits the vein snugly if too large it will be difficult to move freely and will excite venospasm if too small bleeding will be troublesome As a rule size 8 is best for adults with good veins no 7 for children and adults with small veins and no 6 for smaller children The larger the catheter the easier it is to see a point of some importance when the heart is large A no 6 catheter is also advised for cases of severe pulmonary stenosis with normal aortic root when there is some danger of a large catheter blocking the pulmonary outflow

When all is ready the vein is opened and the catheter which has been previously washed inside and out with saline to *remove all traces of* formalin and to the hilt of which is attached a 5 or 10 ml syringe loaded with saline is inserted in the manner of introducing a cannula and pushed up the vein its curved tip being directed medially and care being taken to avoid introducing air Any obstruction can usually be overcome by rotating the catheter a little one way or the other When the tip is judged to be in the neighbourhood of the superior vena cava the lights are turned out 5,000 units of heparin are given through the catheter and the inelastic sterile tube which will connect the catheter with the electromanometer is set up ready for use while the operator is accommodating the rest of the procedure being under fluoroscopic control Kinks at the thoracic inlet may be passed during deep inspiration abducting the arm or altering the position of the head and neck are usually a waste of time If the obstruction appears insuperable it can be overcome by allowing the tip of the catheter to enter the jugular and to rotate it this way or that until some resistance is felt if then the catheter is pushed gently forwards a loop will form near the tip and this is encouraged until the bend itself passes down the superior vena cava In over 1 000 pulmonary artery catheterisations the right superior vena cava has never be[...] sent and if there was no clini

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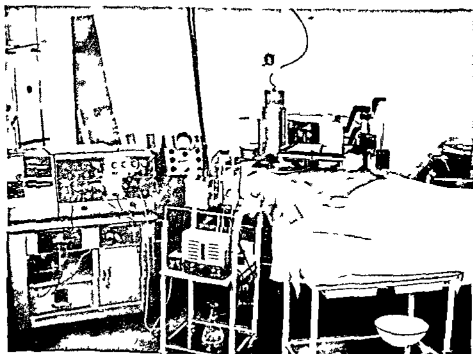


Fig 5 08—Photograph of the N E P multichannelled recorder Sanborn electromanometer and cathode ray monitor used for cardiac catheterisation at the Institute of Cardiology





(a) Anterior view
(b) First oblique position
(c) Second oblique position

Fig 5 10—Catheter in right pulmonary artery




(a) Anterior view
(b) First oblique position

Fig 5 11—Catheter in the left pulmonary artery



Fig 5 11(c)—Catheter in left branch of the pulmonary artery (2nd oblique position)



Fig 5 12—Showing a catheter in the left upper pulmonary vein after passing through a foramen ovale in a normal subject

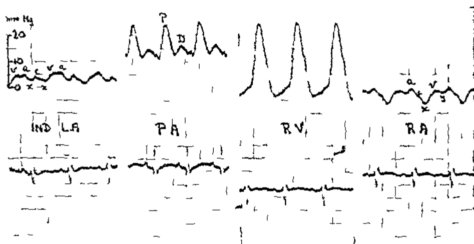



Fig 5 13—Normal pressure pulses from the left atrium (indirect) pulmonary artery right ventricle and right atrium

evidence of thrombosis the vessel has never been blocked With the aid of deep inspiration and this easily formed loop difficulty in entering the superior vena cava has been overcome in all cases

As soon as the catheter lies in the right atrium its hilt should be connected to the electromanometer and the right atrial pressure pulse recorded simultaneously with the electrocardiogram The variable hydraulic damper is then adjusted and the recording system tested while the operator accommodates more thoroughly Direct writing multichannel recorders have proved very satisfactory for routine diagnostic work if a photographic recording system is used it is imperative to have a cathode ray monitor as well so that tracings can be inspected continually The zero reference point to which the manometer is adjusted may be the sternal angle or a measured distance such as 10 cm above the surface of the couch which represents the expected level of the heart itself There is some advantage in incorporating a high pressure very slow heparinised saline drip in the hydraulic system to combat any possibility of clotting in the lumen of the catheter but with due care thrombosis can be avoided without it Blood should never be allowed to enter the catheter inadvertently and when deliberately withdrawn (as in sampling) or when assumed to have entered (as when advancing into a high pressure zone with the hilt of the catheter attached to an unattended syringe) it should be cleared as soon as possible by injecting saline from the syringe This is not only to avoid clotting but also to prevent particles of blood becoming enmeshed in the weave with which the catheter is lined—a fruitful source of future pyrogens and rigors

The best way to enter the right ventricle from the right arm is to allow the tip of the catheter to impinge against the lateral wall of the right atrium and by pushing on to form a loop there when rotated medially this loop ensures that the tip of the catheter is directed upwards when it passes through the tricuspid valve and so passes on readily into the pulmonary artery (fig 5 09) The position of the catheter is determined by fluoroscopy by the pressure pulse recorded and if necessary by sampling For example if the tip of the catheter looks as if it were in the outflow tract of the right ventricle but will not pass onwards the pressure pulse will probably be atrial in form and a blood sample may be bright red from the left atrial appendix or almost black from the coronary sinus

Typical positions are illustrated in figures 5 10 to 5 12 and a normal series of pressure pulses in figure 5 13 As previously mentioned an indirect left atrial pressure pulse may be obtained by wedging the tip of the catheter in a distal branch of the pulmonary artery so that a little force is required to withdraw it If the catheter can be passed through a patent foramen ovale or atrial septal defect an indirect pulmonary artery pressure tracing may also be recorded by wedging the catheter in a pulmonary vein (fig 5 14)

Samples of blood (5 ml ) are withdrawn under paraffin from all important positions which the catheter has entered preferably in quick

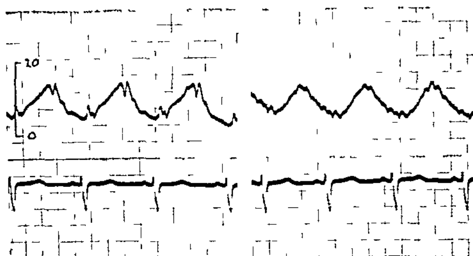



Fig 5 14—Pulmonary artery pressure pulse recorded indirectly by wedging a catheter in a pulmonary vein

and an arterial sample is obtained simultaneously with that from the pulmonary artery The samples are expelled from the syringe by means of a long needle or cannula into the bottom of small glass vessels containing a bead of heparin under a layer of liquid paraffin In both the syringe and container the paraffin keeps the samples free from contact with air They *should be analysed for oxygen content or unsaturation by means of* Van Slyke s or Haldane s method respectively as soon as possible if blood gas analysis is delayed for several hours the samples should be stored in a refrigerator

The *total screening time* should not exceed 30 minutes at 1 m a

On withdrawing the catheter the vein is usually ligated attempts to save its lumen by passing skin sutures under the vein above and below the opening in its wall have been none too successful and occasionally appreciable hæmorrhage has occurred

*Complications*

VENOSPASM often proved troublesome in the early days it has been *practically abolished by efficient local anæsthesia and by selecting a catheter* that is not too large for the vein Its present 2 per cent incidence seems to be associated with inadequate sedation in unduly nervous individuals or improper washing of the catheter so that traces of formalin still remain on its surface

ECTOPIC BEATS are extremely common and may be disregarded They occur especially when the tip of the catheter lies in the body of the right ventricle

PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA, usually 2–1 auricular flutter occurred in 3 3 per cent of 1 000 cases catheterised at the National Heart Hospital or Brompton Hospital It occurred in 11 4 per cent of 88 cases of atrial septal defect in 9 per cent of 45 cases of ventricular septal defect but not more frequently than in normal subjects (4 per cent of 50 cases) in any other condition For example it occurred in 2 4 per cent of 335 cases of mitral valve disease and in 2 per cent of 145 cases of pulmonary stenosis with normal aortic root It did not occur at all in 60 cases of patent ductus in 75 cases of Fallot s tetralogy nor in 48 cases of pulmonary hypertension with reversed shunt

PAROXYSMAL VENTRICULAR TACHYCARDIA is fortunately rare (1 per cent) although short bursts of ventricular ectopics are common enough

VENTRICULAR FIBRILLATION occurred in three cases once in Ebstein s disease once in advanced atrial septal defect and once in primary pulmonary hypertension it resulted in immediate death in two of them giving a mortality rate of 0 2 per cent for the whole series

TRANSIENT RIGHT BUNDLE BRANCH BLOCK occurred in 5 per cent In one such instance in which permanent left bundle branch block was already present this resulted in 2–1 heart block and might well have been serious Since then left bundle branch block has been considered a contraindication to catheterisation

TRANSIENT NODAL RHYTHM developed in 1 5 per cent and was inconsequential

AIR EMBOLISM could occur if the operator was careless and might have dire consequences in cases with right to left shunt None was recognised in this series however but particular care has always been taken to keep the hilt of the catheter below right atrial level when sampling

THROMBO EMBOLISM was also totally avoided although clotting in the catheter occurred in 1 per cent This was nearly always the fault of the operator and should have been prevented Subsequent phlebothrombosis was not uncommon but pulmonary embolism was very rare (0 05 per cent) and never serious Such cases however were treated with heparin and dindevan

CEREBRAL ABSCESS which may have been due to paradoxical embolism occurred in two cases of Fallot s tetralogy one just before catheterisation was about to be undertaken the other a month afterwards

RIGORS due to pyrogens washed out of improperly cleaned catheters in which blood had been allowed to lie too long on a previous occasion were very troublesome indeed before the catheters were treated with a hydrogen peroxide drip after use There have been only two in the last 500 cases

SYNCOPE due to blocking the outflow tract of the right ventricle with the catheter at valve or infundibular level occurred in three cases of severe pulmonary stenosis with normal aortic root two with reversed interatrial shunt an incidence of about 6 per cent but in no other condition Vasomotor syncope associated with anxiety occurred twice in the series

WOUND SEPSIS has never been serious but can be a nuisance to both patient and staff its frequency is naturally inversely related to the amount of care and trouble spent on proper aseptic precautions

*Contra indications*

1 Cases of known *ischæmic heart disease* should not be catheterised at all under any circumstances Three instances are known to the author one died immediately from ventricular fibrillation the other two both developed paroxysmal ventricular tachycardia and the procedure was abandoned

2 *Ebstein s disease* is dangerous Out of six I have personally catheterised one died immediately from ventricular fibrillation and one developed paroxysmal tachycardia which could have been ventricular I know of two other deaths amongst the relatively few cases of Ebstein s disease in the world that have been catheterised

3 Cases with *left bundle branch block* run a 5 per cent risk of developing transient bilateral branch block which could well result in complete heart block

4 Cases of *advanced atrial septal defect* with gross dilatation of the right side of the heart need very careful handling one of the two deaths in the series here analysed occurred in such a case and another is known to the author

5 Advanced *anoxic cor pulmonale* has been responsible for at least one death from cardiac catheterisation

In a review of 973 catheterised cases Hebert Scebat and Lenegre found the mortality was 0 7 per cent Two of the deaths were due to cardiac hæmorrhage from trauma two to severe rigors one to acute pulmonary œdema and three to subsequent pulmonary embolism *Acute pulmonary œdema* occurred in 14 of their series cases of mitral stenosis in which the pulmonary vascular resistance is judged to be low should be treated with great respect preliminary dehydration is important and the X ray couch should be tiltable foot down

A mortality rate of 0 2 per cent in 1 000 cases was reported by Zimdahl (1951) and of 0 1 per cent in 5 691 cases by Cournand *et al* (1953)

*Normal pressures*

There were 50 normal subjects amongst the 1 000 catheterised The figures given here are based on these The reference point to which the pressures are related is the sternal angle so that they are all 3 to 5 mm Hg lower than those generally reported

*The right atrial pressure* averaged −0 5 −4 −1 5 −1 mm Hg for *a x v* and *y* respectively the average mean pressure being −1 3 mm Hg with reference to the sternal angle The range of the mean pressure was +2 to −5 The significance of *a x v* and *y* has already been discussed (p 47)

*The indirect left atrial pressure* averaged 4 mm Hg higher with little to choose between *a* and *v* or *ac* and *v* in good tracings sound artifacts made

precise measurements difficult at these low pressures

*The right ventricular pressure* averaged 16/—1 with a mean of 4 mm Hg The highest systolic pressure recorded was 25 mm Hg very few being over 20 and only one under 10

*The pulmonary artery pressure* averaged 16/7 mm Hg and the mean 11

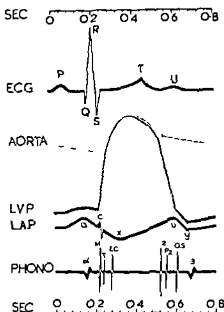



Fig 5 15—Time relationships between electrocardiogram aortic left ventricular and left atrial pressure pulses and the phonocardiogram (see text)

*Time relationships of central pressure pulses* (fig 5 15)

The first recordable event in the cardiac cycle is the right atrial or first half of the P wave of the electrocardiogram The *a* wave of the right atrial pressure pulse begins at the peak of P and reaches the jugular pulse about 0 1 second later

The *x* descent due to atrial relaxation begins before ventricular systole and is interrupted by a notch or deformity representing closure of the tricuspid valve this is the right atrial *c* wave It is rarely large enough to be seen in the jugular pulse

The left atrial *c* wave is synchronous with the onset of left ventricular systole with the mitral element of the first heart sound and with the S wave of the electrocardiogram The right atrial *c* wave probably occurs 0 02 to 0 03 second later and is synchronous with the onset of right ventricular systole and with the tricuspid component of the first sound

The *x* descent of the right atrial pressure pulse continues after the *c* interruption the systolic part of the trough being partly attributed to descent of the base the atrio ventricular septum moving downwards and to the left towards the apex of the heart as the ventricles contract so creating negative pressures in the atria

*Isometric ventricular contraction* is that part of ventricular systole that occupies the time interval between closure of the tricuspid and mitral valves and the opening of the pulmonary and aortic valves respectively a matter of 0 04 to 0 05 second

*The opening of the semi lunar valves* which signals the end of the isometric contraction phase occurs about 0 03 second before the vascular components of the first heart sound These are normally inaudible but under certain circumstances they can be heard as systolic ejection clicks

Thus the time interval between the mitral component of the first heart sound and an aortic ejection click is a measure of the duration of left ventricular isometric contraction if 0·03 second delay is allowed (Leatham 1954)

*The ejection phase* then begins and lasts about 0·25 second two thirds of the ventricular stroke volume are pumped into the great vessels during the first half of this period (Wiggers 1921) The carotid pulse and the carotid *c* wave of the jugular phlebogram follow left ventricular ejection by about 0·03 second and the radial pulse is some 0·10 second later (Lewis 1925)

*Protodiastole* is the short period of ventricular relaxation between the end of the ejection phase and closure of the semilunar valves The aortic valve normally closes before the pulmonary and synchronises with the first component of the second heart sound and more or less with the end of the T wave of the electrocardiogram

*The isometric relaxation phase* is the time occupied by the ventricles between closure of the semilunar valves and the opening of the atrio ventricular valves (0·06 to 0·10 sec ) The two components of the second heart sound signal its onset in respect of each ventricle (P falling 0·02 to 0·05 second after A ) and the top of the *v* waves of right and left atrial pressure tracings signal its end in respect of each ventricle The opening snap of mitral stenosis also synchronises with the end of left ventricular isometric relaxation in that disease

After the opening of the mitral and tricuspid valves atrial and ventricular diastolic pressures fall together this is the *y* descent or downstroke of *v* seen in atrial pressure pulses The subsequent rise of diastolic pressure in both atria and ventricles depends on the venous pressure gradient and the tone of the ventricles As used here ventricular tone may be defined as resistance to diastolic filling Since the left atrial pressure averages 4 mm Hg higher than the right it must be assumed that the left ventricular diastolic pressure is also 4 mm Hg higher than the right and this may be a function of tone

From these time relationships it may be observed that if the heart rate is 60 beats per minute allowing 1 second for the length of each cycle the ventricles are allotted 0·62 second in which to fill and 0·28 second in which to contract, 0·10 second being expended in protodiastolic and isometric relaxation

*Normal samples*

*The oxygen capacity* is the total amount of oxygen held by a litre of blood when fully saturated Since 1 G of hæmoglobin will hold 1·34 ml of oxygen at normal temperature and pressure a litre of normal blood will hold $15 \times 1{\cdot}34 \times 10 = 201$ ml of oxygen when fully saturated

*The arterial oxygen saturation* is normally 95 per cent of its oxygen capacity This means that a litre of normal arterial blood holds $\frac{95}{100}$ of 201 = 191 ml of oxygen

Samples of arterial blood may be obtained from the brachial or femoral artery by direct puncture A sharp short bevelled 18 gauge needle attached to an all glass syringe containing a little paraffin should be plunged into the vessel The arterial blood pressure then lifts the barrel of the syringe spontaneously little aspiration being necessary On withdrawing the needle the site of puncture should be compressed digitally for at least a minute

*The oxygen content* of a sample is the actual amount of oxygen it contains and may be measured by means of Van Slyke s apparatus Thus the oxygen content of normal arterial blood in the example given above is 191 ml per litre This is sometimes expressed as 19 1 volumes per cent

*The oxygen unsaturation of a sample* is its oxygen capacity less its oxygen content and may be measured by means of Haldane s apparatus Thus the normal arterial oxygen unsaturation is around 10 ml per litre or 1 volume per cent

*The arterio venous oxygen difference* averaged 34 ml per litre in our series of 50 normal subjects, the range being 21 to 48

*The cardiac output* calculated from Fick s formula (q v ) averaged 8 6 litres per minute the range being 5 8 to 12 8 These figures are not basal but they certainly represent what is actually found under the conditions inevitably associated with cardiac catheterisation The *basal cardiac output* is said to be around 4 to 5 litres per minute and is about a litre higher in the horizontal than in the erect position (McMichael and Sharpey Schafer 1944) The *cardiac index* is the cardiac minute output per square metre of body surface and should be around 3

*Samples from the right side of the heart* (superior vena cava right atrium right ventricle and pulmonary artery) should not differ by more than 5 per cent in oxygen saturation the scatter being centred around a mean difference of 3 per cent in our series The *average oxygen saturation* of all these samples was 75 per cent the vast majority being between 70 and 80 per cent

The *pulmonary vascular resistance* (q v ) averaged 1 unit or 80 dynes sec/cm$^{5}$, commonly ranging between 0 5 and 1 5 units The maximum normal resistance was 2 5 units

## OXIMETRY

Photovoltaic iron selenium ear oximeter are based on the principle that oxyhæmoglobin and reduced hæmoglobin absorb light differently Two cells are used One is covered by a green wratten 61 N filter which responds to light with wave lengths of 480 to 600 millimicrons and 750 to 800 millimicrons the intermediate part of the spectrum being filtered out Both oxy and reduced hæmoglobin transmit light of these wave lengths equally

so that the output of this cell depends on the thickness of the ear and the amount of blood in it The second cell is covered by a red Wratten 29 F filter which transmits light with wave lengths of 600 millimicrons and above Since this red portion of the spectrum is absorbed in much greater degree by reduced hæmoglobin than oxyhæmoglobin the amount of light activating this cell is proportional to the percentage of oxyhæmoglobin present in the blood through which the light passes the first cell balancing the second in respect of other variables (Millikan 1942)

## RESPIRATORY FUNCTION TESTS

An elementary knowledge of respiratory physiology is essential to a proper understanding of the circulation

### *CHEMICAL AND NERVOUS CONTROL OF BREATHING*

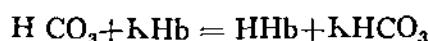
When discussing the causes of dyspnœa it was observed that the respiratory centre reacted to several independent stimuli and that the total response depended on the algebraic sum of these stimuli (Gray 1950)

ANOXIA (as diminished oxygen tension in the plasma) is a relatively weak stimulus which acts on chemoreceptors in the carotid sinus and aortic bodies (like sodium cyanide lobeline and coramine) alone it is barely capable of doubling ventilation An increased oxygen tension in the plasma (p O ) does not inhibit respiration Oxygen tension of course is an expression of the amount of oxygen dissolved in the plasma and in arterial blood is nearly equal to the partial pressure of oxygen to which the plasma has been exposed in its journey through the lungs i e to the partial pressure of oxygen in alveolar air The partial pressure of oxygen in the atmosphere is about 21 per cent of the barometric pressure = 21 per cent of 760 mm Hg = 159 mm Hg In alveolar air the gas mixture is not the same as in the atmosphere for it is almost fully saturated with water vapour contains about 5 6 per cent of carbon dioxide which it has collected from the plasma and is left with only 14 2 per cent of oxygen The partial pressure of oxygen in alveolar air should therefore be 14 2 per cent of 760 mm Hg or allowing for water vapour 14 2 per cent of (760−47) = 101 2 mm Hg That the arterial oxygen tension (90 to 95 mm Hg) is not the same is due to slight perfusion of unventilated alveoli The oxygen tension of venous blood is only about 40 mm Hg so that there is a strong oxygen pressure gradient across the interface between the alveolar wall and the proximal end of the pulmonary capillary favouring rapid diffusion The plasma oxygen tension determines whether hæmoglobin takes up oxygen or releases it The familiar oxygen dissociation curve of hæmoglobin shows the changing affinity that hæmoglobin has for oxygen according to the oxygen tension of the plasma at high tensions around 100 mm Hg hæmoglobin is 95 per cent saturated with oxygen, as the tension falls towards 70 mm Hg the proportion of oxyhæmoglobin declines very little

to about 90 per cent as the oxygen tension falls below 70 mm Hg however hæmoglobin appears more and more in its reduced form so that at an oxygen tension of 40 mm Hg, which is average for venous blood hæmoglobin is only about 70 per cent saturated and at a tension of 30 only about 50 per cent saturated this behaviour makes hæmoglobin an ideal vehicle for transporting oxygen storing it when plentiful and releasing it where it is most wanted

CARBON DIOXIDE stimulates the respiratory centre directly and is capable of increasing ventilation tenfold Again it is the tension of carbon dioxide in the arterial blood (p $CO_2$) that matters and this is equal to the partial pressure of carbon dioxide in alveolar air for this gas diffuses far more rapidly in fluid media than oxygen The partial pressure of alveolar CO is normally about 5 6 per cent of (760−47) mm Hg = 40 mm Hg approximately Thus the arterial $CO_2$ tension is also 40 mm Hg A rise of only 2 5 mm Hg in arterial CO tension is enough to double ventilation (Gray 1950) a fall in p CO depresses the respiratory centre

Like oxygen carbon dioxide is formed in too great a quantity to be transported as a simple solution in plasma and so it too has a special means of conveyance Hæmoglobin is again made use of Carbon dioxide from the tissues diffuses into the venous blood at a tension around 46 mm Hg and readily enters the red corpuscles Here with the aid of an enzyme carbonic anhydrase it joins with water to form carbonic acid $H_2CO_3$ This combines with potassium base obtained from reduced hæmoglobin thus



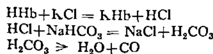
$$H\ CO_3 + KHb = HHb + KHCO_3$$

because carbonic acid is a stronger acid than reduced hæmoglobin Dissociation allows bicarbonate anions ($HCO_3$) so formed in the cells to diffuse out into the plasma leaving unattached potassium kations (which cannot pass the cell membrane) within the corpuscles Equilibrium is restored by the well known chloride shift dissociation of sodium chloride in the plasma allowing sodium+ to combine with $HCO_3$ to form plasma bicarbonate, while chloride anions pass into the red cells to combine with potassium



$$K^+\ HCO_3^- \qquad Na^+\ Cl^-$$
$$KCl \qquad NaHCO_3$$

When the red cells reach the lungs the chloride shift is reversed because oxyhæmoglobin is a much stronger acid and promptly re acquires the potassium base thus releasing chloride from the cells the chloride combines with the sodium of the plasma bicarbonate to form the weaker acid $H\ CO_3$ from which carbon dioxide is finally excreted through the lungs thus



$$HHb + KCl = KHb + HCl$$
$$HCl + NaHCO_3 = NaCl + H_2CO_3$$
$$H_2CO_3 \rightarrow H_2O + CO$$

It follows that *an increase of carbon dioxide in the blood results in an increase of*

*plasma bicarbonate* When the carbon dioxide of the body is depleted as by forced breathing the plasma bicarbonate falls In other words *carbon dioxide is carried as bicarbonate* in the plasma

Since the plasma bicarbonate is the most important buffer substance available for neutralising fixed acid such as lactic acid it has been called the *alkali reserve* This may be measured by finding out how much carbon dioxide is liberated from the plasma under controlled conditions when exposed to an acid the answer being expressed in volumes (ml) per cent The normal *carbon dioxide content* of plasma is 53 to 75 volumes per cent when measured in this way This is often called the *carbon dioxide combining power* or *carbon dioxide capacity* of the plasma The terms *acidosis* and *alkalosis* refer to states in which the carbon dioxide content of the plasma is below 53 or above 75 volumes per cent respectively This has caused much confusion for every clinician knows that forced breathing which results in $CO_2$ washout causes a transient slight rise in pH (alkalæmia) yet the reduction in alkali reserve (carbon dioxide content) to which it also gives rise, entitles it to be called a state of acidosis Again in advanced cor pulmonale particularly if ventilation is depressed by any means a high $CO_2$ tension may be associated with a lowered pH (acidæmia) and increased alkali reserve (alkalosis) The confusion would be avoided if the terms acidæmia and alkalæmia were used (as now) to denote a fall or rise of pH and the terms acidosis and alkalosis were dropped altogether in favour of more precise designations for the plasma bicarbonate

A less variable and more informative figure is the carbon dioxide content of arterial blood which in health is 45 to 53 ml per cent

A final very important point about the carbon dioxide tension as a respiratory stimulant is the narcotic effect produced when the tension exceeds 60 mm Hg At such levels carbon dioxide may not only cause unconsciousness but actually depresses the respiratory centre As will be seen later the treatment of cor pulmonale with oxygen is much influenced by this consideration

THE HYDROGEN ION CONCENTRATION or pH value is the third important respiratory stimulant and like carbon dioxide acts directly on chemo receptors in the respiratory centre The normal pH is given as 7 41 it remains remarkably constant in health and is one of the last things to alter in disease It is maintained largely by the buffer systems of the blood by removal of an ever varying quantity of carbon dioxide by the lungs and by excretion of acid or alkaline substances in the urine The chief effect of the buffer systems such as the plasma bicarbonate is to ensure as far as possible that no acid stronger than $H_2CO_3$ can exist in the blood For example lactic acid derived from working muscle is at once converted by sodium bicarbonate into sodium lactate and carbonic acid Any increase of $CO_2$ tension resulting from the exchange at once stimulates the respiratory centre and excess $CO_2$ is removed via the lungs Nevertheless metabolic disturbances do occur in diabetes mellitus for example in which a reduced

pH causes hyperventilation in such cases the carbon dioxide tension will also be reduced (as a result of increased $CO_2$ washout) An increased $CO_2$ tension itself also causes slight reduction of the pH

MUSCULAR EXERCISE is a respiratory stimulant independent of secondary changes in $CO_2$ tension

HEAT is also an important respiratory stimulant Thermoreceptors in the hypothalamus react to changes in body temperature and explain the hyper ventilation of high fever Thermoreceptors in the skin react to change in the temperature of the environment

The *inter relationships* between these various respiratory stimuli are complicated and cannot be discussed here but when considering the effect of any one of them it is most important to consider at the same time what is happening to the others For example with very high CO tensions in advanced cor pulmonale, the respiratory centre may be responding only to oxygen lack as previously explained If the patient is nursed in an oxygen tent the only stimulant to respiration may be abolished and ventilation may greatly decline This reduces excretion of carbon dioxide and the patient may become unconscious from CO narcosis

So much then for the central control of respiration We now have to consider the physiology of ventilation itself, i e the events that take place in the lungs to ensure proper oxygenation of perfusing blood and elimination of carbon dioxide

## VENTILATION

In what is called a *steady state* the amount of oxygen taken up by the lungs exactly equals the amount utilised by the tissues minute by minute and the amount of carbon dioxide eliminated by the lungs exactly equals that formed in the tissues The amount of oxygen consumed varies with the surface area of the body, which can be obtained from tables of height and weight and is called the metabolic rate It is usually around 250 ml per minute, and if measured under basal conditions is called the *basal metabolic rate* being expressed as a percentage of normal To every 250 ml of oxygen consumed, about 200 ml of carbon dioxide is eliminated The ratio in this example $\frac{200}{250} = 0\ 80$ is called the *respiratory quotient*

### *Resting ventilation*

For each 100 ml of oxygen consumed about 2 5 litres of air must be breathed This ratio is the *ventilation equivalent for oxygen* If 250 ml of oxygen have to be absorbed per minute, then at this equivalent 6 25 litres *of air must* be breathed This is the resting ventilation and is the *tidal volume* (about 500 ml ) multiplied by the number of inspirations per minute (in this case 12 5) and can be measured very simply with

It is the respiratory analogy of the cardiac output at -

*Reserves*

From a state of quiet breathing it is always possible to inspire much more deeply this extra depth of a single maximum inspiration is the *inspiratory reserve* (2 to 2 5 litres) The term *inspiratory capacity* (or complemental air) refers to the sum of the tidal volume and the inspiratory reserve it is the maximum inspiration after quiet expiration The *expiratory reserve* (or supplemental air) is the maximum volume of air that can be expelled after quiet expiration (usually 1 to 1½ litres)

*Vital capacity*

The sum of the tidal inspiratory reserve and expiratory reserve volumes is the vital capacity It should measure around 3 5 to 4 5 litres

*Total lung volume (or capacity)*

After maximum expiration there is still a good deal of air in the bronchial tubes and trachea this is known as the dead space or *residual volume* and in disease may include parts of the lung that cannot be deflated It is possible to measure the dead space plus the expiratory reserve volume during quiet breathing the sum of the two being called the *functional residual capacity* (air or volume) by finding out how much a known quantity of an inert gas such as helium is diluted when introduced into a closed circuit comprising the air in the spirometer and the space to be measured The residual volume of course is the functional residual capacity so determined less the expiratory reserve volume as measured directly with a spirometer The *total lung volume* is the residual volume plus the vital capacity or the functional residual capacity plus the inspiratory capacity In health the residual volume measures 1 to 1½ litres and the total lung volume about 5 litres The various divisions of the lung volume are shown diagramatically in figure 5 16 A useful ratio is the residual volume expressed as a percentage of the total lung capacity (normal 20 to 25 per cent) According to Motley (1950) this measurement correlates well with the degree of emphysema present

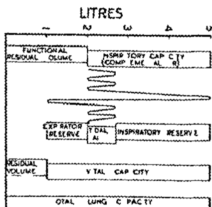



Fig 5 16—Subdivisions of the lung volume

*Maximum breathing capacity*

One of the most important measurements of lung function is the maximum breathing capacity which is the maximum volume of air that can be ventilated per minute It can be measured with a spirometer provided sufficient attention is paid to eliminating resistance Maximum

forced breathing is continued for 15 seconds and the result expressed in litres per minute There is a wide normal range scattering around 75 to 100 litres per minute

The *breathing reserve* is the maximum breathing capacity less the resting ventilation per minute As pointed out by Donald (1953) much of this so called reserve can never be used for even normal subjects are uncomfortably dyspnœic when using 50 to 60 per cent of their maximum breathing capacity It may be better simply to express the actual ventilation per minute as a percentage of the maximum breathing capacity

*Mixing efficiency*

In normal lungs all functioning alveoli are ideally supplied with an equal quantity of inspired air and each is perfused with blood from the pulmonary arteries non functioning alveoli are collapsed and are not perfused related capillaries temporarily shutting down In disease, however this is not necessarily so unperfused alveoli may be supplied with air and perfused alveoli may not be so supplied When all parts of the lung are properly ventilated an inert gas like helium when introduced to a closed spirometer lung circuit quickly attains uniform distribution after which no further dilution occurs If parts of the lung contain stale air which is not moved to and fro however efficient mixing is delayed, and dilution of helium takes longer to reach a static level The speed at which an inert gas attains maximum dilution is therefore a measure of mixing efficiency but allowance must be made for a number of variables which influence the rate of mixing such as the minute volume of respiration at the time (Bates and Christie 1950)

Unventilated perfused alveoli necessarily lead to a fall in oxygen tension and content of arterial blood But a similar degree of oxygen unsaturation of arterial blood may result from difficulty in oxygen diffusion across the interface between alveolus and capillary as in diffuse fibrosis of the lung In this group of cases however mixing efficiency is normal

*Poorly ventilated space*

When the concentration of helium is plotted against time in normal subjects a smooth dilution curve is constructed which at first falls away rapidly and then gradually straightens out until horizontal When mixing is inefficient owing to parts of the lung being underventilated rapid dilution is checked early the initial steep slope suddenly assuming a more gentle gradient This point signals complete mixing in all properly ventilated parts of the lung the rest of the curve representing slower mixing in poorly ventilated spaces From the concentration of helium at the moment its dilution is checked the volume of properly ventilated lung can be calculated this subtracted from the total lung volume gives the volume poorly ventilated space

*Diffusion gradients*

Owing to the extremely high rate of carbon dioxide diffusion in fluids, the arterial p $CO_2$ is always virtually the same as that in the alveoli (Riley and Cournand, 1951) The oxygen tension in the alveoli and the p $O_2$ of blood leaving the pulmonary capillaries however is not necessarily the same although it has been shown to be so in health (Lilienthal *et al* 1946) minor differences between alveolar and arterial p $O_2$ being due to slight *venous admixture* i e to a little perfusion of unventilated alveoli

The alveolar oxygen tension may be calculated from the formula

$$\text{Alveolar p } O_2 = \text{p } O_2 \text{ in inspired air} - \frac{\text{alveolar p } CO_2}{\text{resp quotient}}$$

as quoted by Donald (1953) This formula is based on two important observations (1) the differences in partial pressure between $O_2$ and $CO_2$ in the inspired air and alveolar air are proportional to the quantities of these gases consumed and excreted so that

$$\text{R Q or } \frac{CO_2 \text{ eliminated}}{O_2 \text{ absorbed}} = \frac{\text{alv p } CO_2 - \text{insp p } CO_2}{\text{insp p } O_2 - \text{alv p } O_2}$$

and since the partial pressure of $CO_2$ in inspired air is negligible

$$\text{R Q} = \frac{\text{alv p } CO_2}{\text{insp p } O_2 - \text{alv p } O_2}$$

and (2) the alveolar $CO_2$ tension is the same as that in arterial blood as previously stated so that

$$\text{R Q} = \frac{\text{arterial p } CO_2}{\text{insp p } O_2 - \text{alv p } O_2}$$

$$\text{Alv p } O_2 = \text{insp p } O_2 - \frac{\text{art p } CO_2}{\text{R Q}}$$

Now the partial pressure of oxygen in the inspired air which is fully saturated with water vapour is about 21 per cent of $(760-47) =$ 150 mm Hg Thus in normal subjects

$$\text{the alveolar oxygen tension} = \text{(say) } 150 - \frac{40}{0\,8} \text{ mm Hg}$$
$$= 100 \text{ mm Hg}$$

Assuming the arterial oxygen tension is 95 mm Hg this gives an alveolar arterial oxygen tension gradient of 5 mm Hg which represents the admixture of a small quantity of unventilated perfused venous blood

The technique of these measurements of lung function must be sought in standard works on lung physiology The basic principles involved and the terminology employed have been described here in some detail in order to help clinicians understand what the respiratory physiologist is about and what the various respiratory tests to which his patients may be subjected really mean

*APPLICATIONS*

Briefly *emphysema* is as a rule characterised by a normal or even increased total lung volume increased residual volume diminished vital capacity diminished inspiratory reserve greatly diminished maximum breathing capacity increased resting ventilation poor mixing efficiency large poorly ventilated space and in advanced cases by reduction of arterial oxygen tension and saturation and an increase of arterial carbon dioxide tension and content

*Pulmonary fibrosis* in various forms is characterised especially by a raised alveolar arterial oxygen tension gradient and in advanced cases by a reduced arterial oxygen saturation ventilation being more or less normal and the arterial $CO_2$ content normal or low

*Pulmonary venous congestion* ' from left heart failure or mitral stenosis behaves rather like pulmonary fibrosis in respect of its effect on lung function

*Bronchospasm pneumonia atelectasis large pleural effusion spontaneous pneumothorax* and other space filling lesions interfere chiefly with ventilation

## RENAL FUNCTION TESTS

*Testing the urine* for albumin and sugar microscopic examination of the urinary sediment (particularly for red cells and casts) bacteriology when indicated urine concentration te ts blood urea urea concentration and clearance and intravenous pyelography usually give sufficient information to satisfy the cardiologist but the glomerular filtration rate as measured by inulin or creatinine clearance and the plasma blood flow as measured by diodone or para amino hippuric acid clearances are useful refinements Renal function is particularly important in all hypertensive states congestive heart failure bacterial endocarditis and certain collagen diseases

The *water concentration test* consists simply of withholding all fluids for a maximum of 36 hours (starting at 6 p m ) or until the specific gravity of the urine is 1027 at room temperature This is a very simple yet sensitive test of the power of the tubules to reabsorb water The more damaged the kidney in hypertension the more nearly does the urine resemble the glomerular filtrate and in the end its specific gravity is the same as that of the plasma being fixed at 1010

*Urea concentration* is another test of tubular function After ingesting 15 G of urea a normal individual should pass urine having a urea concentration of at least 2 G per cent The dose is taken immediately after emptying the bladder and urine is then voided after one and again after two hours the second specimen being the more important since diuresis may interfere with concentration during the first hour

A *blood urea* higher than 45 mg per cent indicates considerable impairment of glomerular filtration In uremia of course it may rise as high as 500 mg per cent The *blood creatinine* normally 0 7 to 2 mg per

rises sharply in uræmia, and may reach 5 or even 10 mg per cent Creatinine is normally concentrated to about 75 mg per cent in the urine

A *clearance test* measures the amount of blood or plasma passing through the glomeruli or tubules which is cleared of a particular substance per minute In the familiar urea clearance test of Van Slyke the concentration of urea in the blood and urine, and the volume of urine formed each minute are measured suppose the urine flows at a rate of 2 ml per minute and each ml contains 20 mg of urea (concentration 2 G per cent) then the quotient 40 mg per minute represents the quantity of urea filtered from the blood If the blood urea at the time was 0 4 mg per ml (40 mg per cent) then the amount of blood filtered of urea must have been $\frac{40}{0\ 4} = 100$ ml Thus we have the simple formula clearance $= \frac{UV}{B}$

where U is the concentration of the substance in the urine
V is the volume of urine formed per minute
and B is the concentration of the substance in the blood

In the case of urea there are two important considerations (1) blood passing through the glomeruli is not completely cleared of urea so that the test does not measure the actual amount of blood passing through the glomeruli but the amount that would have passed had it been totally cleared (2) urea is partly reabsorbed by the tubules particularly when its concentration there is high, as it is likely to be when the urine flow is reduced and under these circumstances Van Slyke found more consistent results were obtained when the formula was changed to

$$\text{urea clearance} = \frac{U\sqrt{V}}{B}$$

The result is expressed as a percentage of normal Average normal urea clearances were found to be 75 ml per minute when the urine flow was 2 ml or more per minute and 54 (using the square root of V in the formula) when the urine flow was less than 2 ml per minute Thus when the *standard* urea clearance is reported as 50 per cent of normal it means that the actual clearance was one half of 54 or 26 ml per minute if the word *maximum* is added it means that the flow was 2 ml per minute or more and that the actual clearance was one half of 75 or 37 5 ml per minute

*Inulin* has the advantage of being filtered freely by the glomeruli but not reabsorbed by the tubules at all (Smith 1939–40) The plasma inulin clearance is measured in exactly the same way, the formula being $C = \frac{UV}{P}$ plasma concentration is substituted for blood concentration because inulin does not penetrate the red cell The average normal plasma inulin clearance is 120 ml per minute This test has another meaning however for since inulin is filtered freely its concentration in the glomerular filtrate is precisely

the same as its concentration in the plasma and since it is not reabsorbed by the tubules the clearance figure determines the amount of filtrate actually formed and may be justly called the *glomerular filtration rate*

*Endogenous creatinine clearance* is also a good test of filtration but not so reliable as inulin (Brod and Sirota 1948) Typical figures are

$$\text{Creatinine clearance} = \frac{UV}{B} = \frac{80 \text{ mg per cent} \times 1\ 5 \text{ ml per minute}}{1 \text{ mg per cent}}$$

$$= 120 \text{ ml per minute}$$

The *total renal blood flow* may be estimated in two ways If the urea content of blood samples from the renal artery and vein are known and the amount of urea excreted in the urine per minute is known then since the amount lost from the blood must equal the amount in the urine

$$\text{renal blood flow} = \frac{UV}{\text{arterio venous urea difference}}$$

$$= (\text{say})\ \frac{2\ 000 \text{ mg per cent} \times 2 \text{ ml per minute}}{30\text{–}26 \text{ mg per cent}}$$

$$= 1\ 000 \text{ ml per minute}$$

Renal vein samples may be obtained by means of venous catheterisation and any substance excreted by the kidney may be used instead of urea In fact urea is not very suitable because of its variable rate of excretion creatinine serves very well

The second method is based on the fact that certain substances like diodone and para amino hippuric acid are totally excreted by the tubules when their blood concentration is sufficiently low so that their clearance rates then genuinely represent the *renal plasma flow* itself (Smith 1939–40)

*Milli equivalents*

The quantity of any substance in whole blood plasma or serum is usually reported in mg per cent or milli equivalents The latter term is used in respect of electrolytes such as sodium potassium and chloride which occur in an ionic form in the plasma The equivalent weight of a substance is that weight of it which will combine with or displace one gramme atom of hydrogen and a milli equivalent is this weight divided by a thousand The equivalent weights of monovalent ions like sodium are the same as their atomic weights e g 23 for sodium so that one *milli equivalent* of sodium weighs 23 mg Thus if the serum sodium is 320 mg

per cent it may be expressed as $\frac{320 \times 10}{23} = 139$ milli equivalent per litres

The advantage of this system is that the unit of any substance is chemically equivalent to the unit of any other substance a statement that would not be true if applied to a unit of metric weight like a milligram

*Electrolytes*

An electrolyte is any substance which in greater or less degree dissociates into its constituent ions when dissolved in water Thus sodium chloride dissociates into sodium cations (positive) and chloride anions (negative) or $Na^+$ $Cl^-$ potassium chloride into $K^+$ $Cl^-$ sodium bicarbonate into $Na^+$ $HCO_3^-$ and so on The most important substances of this kind are sodium, potassium, chloride and bicarbonate and their normal concentrations in the serum are given below

| | *Mg per cent (unless otherwise stated)* | *M eq per litre* |
|---|---|---|
| Serum sodium | 310 to 345 | 135 to 150 |
| Serum potassium | 15 to 21 | 4 to 5 |
| Plasma chlorides | 340 to 390 | 95 to 110 |
| Plasma bicarbonate | 53 to 77 vols of CO per cent | 25 to 35 |

## PHONOCARDIOGRAPHY

Special techniques fall into two major groups those that give information of a kind that cannot be obtained otherwise such as radiology electrocardiography and cardiac catheterisation and those that offer a more accurate or standardised means of measuring or recording phenomena which can be recognised qualitatively in other and usually simpler ways such as sphygmomanometry polygraphy and kymography Although phonocardiography belongs to the second group it has contributed much to our knowledge and understanding of heart sounds and murmurs and has provided us with a practical tool with which to solve difficult auscultatory problems

The heart sounds were first visually recorded by Frank (1904) using a stethoscopic chest piece pneumatic connection mirror capsule (q v ) and optical recording a relatively simple method perfected by Orias and Braun Menendez (1939) Einthoven (1907) substituted a carbon microphone (q v ) for the capsule and let it actuate a string galvanometer More recently the stethoscopic chest piece has been replaced by a Rochelle salt crystal microphone (q v ) which converts sound pressure waves into proportionate electrical charges these are amplified and led to a suitable string or mirror galvanometer (Leatham 1949)

Picked up in this way the intensity of heart sounds and murmurs bears little relation to what is actually heard through a stethoscope low frequency sounds having a very much higher amplitude than high frequency sounds This means that with linear recordings and amplification adjusted so that a high pitched murmur would show suitably in the tracing a low pitched third heart sound would throw the galvanometer beam off the record The human ear is nicely adjusted to this phenomenon and while being

remarkably sensitive to sound frequencies around 2 000 to 3 000 cycles per second it is logarithmically less sensitive to sounds of decreasing frequency until at 15 cycles per second it does not respond at all at the other end of the scale the highest frequency that can be heard is 20 000 to 30 000 cycles per second varying with the individual In phonocardiography it is usually desirable to record not only what is actually heard but also what is on the threshold of hearing Records having a linear response to sound intensity at all frequencies are impracticable, as already explained The intensity of low pitched sounds must be attenuated to bring them more into line with the weaker high pitched sounds so that both may be recorded in the same tracing This is achieved by incorporating filters (condensers and resistances) in the amplifying circuit Three degrees of low frequency attenuations have been found most useful in the first or low frequency response damping of low frequency sounds is minimal and

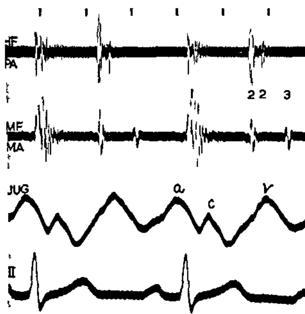



Fig 5 17 —Normal phonocardiogram taken from apex and base recorded simultaneously with the electrocardiogram and the jugular phlebogram Time marking 0 04 and 0 2 sec Split first and second heart sounds best seen in high frequency tracing from the pulmonary area (top graph)

*With acknowledgment to Dr Aubrey Leatham*

amplification has to be reduced so that low pitched sounds such as the third heart sound and soft mitral diastolic murmurs are well seen at the expense of high pitched sounds which may be insufficiently amplified to appear at all in the second or medium frequency record moderate attenuation of low pitched sounds allows greater amplification of high pitched

sounds and murmurs so that these also can be seen in the third or high frequency response, sounds of low frequency are greatly weakened allowing greater amplification and recording of high pitched murmurs This last kind of record is similar to the logarithmic curve of Rappaport and Sprague (1941 1942) and may be called ear like for it closely resembles what is actually heard (Leatham 1949)

The galvanometer must be sensitive to frequencies of at least 1 000 cycles per second preferably to 2 000 if the highest pitched aortic diastolic murmurs are to be recorded faithfully Most systolic murmurs have a frequency around 200 to 400 cycles per second mitral diastolic murmurs 50 to 200 cycles per second and the lower pitched heart sounds 16 to 50 cycles per second (Leatham 1949) Theoretically the cathode ray oscillograph would seem the most suitable instrument for recording heart sounds in view of its almost unlimited frequency response but in practice it has been found less satisfactory partly on account of base line wobble and rather hazy photographs

Phonocardiograms should be recorded simultaneously with an electrocardiogram jugular phlebogram or some other reference tracing so that sounds and murmurs may be accurately timed against recognisable events in the cardiac cycle one of the best reference tracings is actually a second phonocardiogram from a different site (fig 5 17)

The various heart sounds and murmurs that may be recorded in health and disease together with their timing and pitch have already been described in detail in Chapter II and time relationships with other events in the cardiac cycle are illustrated in figure 5 15

## BALLISTOCARDIOGRAPHY

When a gun is fired it recoils This illustrates Newton s third law of motion which states that for every action on a body there is an equal and opposite reaction When a patient with gross aortic incompetence is lying in bed every clinician knows that the bed may rock—footwards during initial systolic ejection and headward as blood courses down the descending aorta As early as 1877 Gordon recorded the movements of a suspended platform on which a man was lying—the first ballistocardiogram Henderson (1905) suggested that there should be a relationship between such recoil movements of the body and the stroke output of the heart The principle was introduced into clinical medicine in 1939 by Starr and his associates Since one of the basic principles of all forms of manometry is that the natural oscillating frequency of a manometer should be well outside the frequency range of the phenomenon being recorded Starr *developed a couch with a natural frequency of 12 to 14* cycles per second when suitably loaded (Starr 1941 1946) which is two and a half times the natural frequency of the human body (3 to 7 cycles per sec ) The bed moves with body recoil such movements being suitably amplified and recorded Nickerson and Curtis (1944) designed a low frequency bed with

a natural oscillation of 1 5 cycles per second critical damping is employed to keep the natural frequency at 1 5 whatever the weight of the patient In the ballistocardiograph designed by Dock and Taubman (1949) the body is allowed to move on its own cushion of fat, the movements of a bar laid across the shins being amplified and recorded A great deal of work particularly in the U S A has been done on the ballistocardiograph in recent years, and has been well reviewed by Scarborough *et al* (1952) and Gubner (1953) An important aspect of this basic research has been the realisation that the forces of acceleration and deceleration are primarily responsible for the ballistic effect

*Clinical ballistocardiogram*

The chief waves of the ballistocardiograms are H I J and K (fig 5 18) H is a relatively small initial headward deflection probably due to venous deceleration at the end of diastole I is the first strong downward deflection and is due to recoil from acceleration of blood in the ascending aorta and pulmonary arteries being synchronous with the rapid ejection phase J is the maximum deflection and is upright it is associated with acceleration of blood in the descending aorta the body recoiling headwards it is synchronous with the main pulse wave of the body K is a fairly strong downward movement and has been attributed to deceleration of blood in the descending aorta due to the impact of the pulse wave at the periphery it disappears in coarctation of the aorta and is augmented in aortic incompetence It must be admitted however that there is no universal agreement about the true origins of these waves

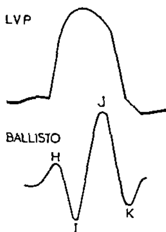



Fig 5 18—Diagram of a normal ballistocardiogram to show approximate time relationship to the left ventricular pressure pulse (see text)

Various formulæ for estimating the stroke output by measuring the height or area occupied by I and J have been devised by Starr and others and modified to give results comparable to those found by methods employing the Fick principle (Scarborough *et al* 1952)

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CHAPTER VI

# DISORDERS OF CARDIAC RHYTHM

THE speed and regularity of the heart beat are controlled by the sino atrial node of Keith and Flack (1907) situated in the upper part of the sulcus terminalis anterior to and to the right of the mouth of the superior vena cava (fig 6 01) Approximately 70 times per minute this node discharges itself and initiates an excitation wave which spreads in all directions over both atria Close to the opening of the coronary sinus above the base of the tricuspid valve on the right side of the atrial

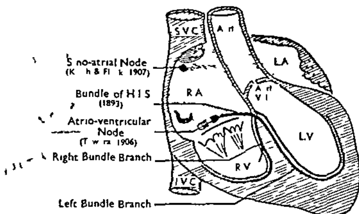



Fig 6 01—Anatomy of the conducting system

septum is situated the atrio ventricular node of Tawara (1906) This also forms impulses but at a slower rate so that normally it is prematurely discharged by the excitation wave initiated by the S A node The impulse then spreads down the Bundle of His which passes horizontally to the left to penetrate the membranous interventricular septum where it divides into left and right bundle branches These pass down each side of the muscular septum just beneath the endocardium The bundle branches then break up into a network of Purkinje fibres which carry the excitatory pro cess to the sub endocardial myocardium

*Physiology of conduction* From the pace maker in the sino atrial node the excitation wave spreads through atrial muscle at a speed of about 1 000 mm per second Passage through the A V nodal tissue is believed to be relatively slow and is estimated at 200 mm per second Spread down the bundle branches and the Purkinje fibres is rapid and is probably as

fast as 400 mm per second Conduction through the ventricles which is believed to proceed directly outwards is put at 400 mm per second (Lewis 1925)

Both the S A and A V nodes are under direct autonomic control being stimulated by sympathetic activity and depressed by vagal activity Cardiac accelerator nerves arise from the lateral horns of the upper 4th or 5th dorsal segments of the spinal cord enter the sympathetic chain and pass cranially to the cervical ganglia Post ganglionic fibres form the superior middle and inferior cardiac nerves which terminate in the S A and A V nodes

## IRREGULARITIES AND ALTERATION OF HEART RATE INITIATED OR GOVERNED BY THE SINO ATRIAL NODE

### *SINUS ARRHYTHMIA*

There is probably no such thing as an absolutely regular heart Slight irregularity the heart quickening with inspiration and slowing with expiration is normal and depends upon variations in vagal tone governed by a reflex which is thought to be initiated by receptors in the lungs Another form of sinus arrhythmia occurs independently of respiration Both are more common in the young and when the heart rate is slow tend to be exaggerated by drugs that increase vagal tone (such as digitalis) and may be abolished by exercise or atropine

Other varieties of sinus arrhythmia are not essentially different but owe their recognition to some particular associated feature thus there is a form

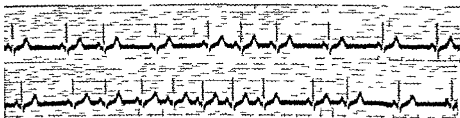


Fig 6 02—Sinus arrhythmia

associated with sino atrial block another with sinus bradycardia and paroxysmal auricular fibrillation or flutter a third with convalescence from certain infectious fevers especially influenza and so on Increased vagal tone is common to all these types

Diagnosis is usually easy or doubt is soon resolved by means of exercise atropine, or amyl nitrite An electrocardiogram provides conclusive evidence (fig 6 02)

Although sinus arrhythmia is normal it should not be regarded as a positive sign of a normal cardiovascular system for it may occur in any form of heart disease

## *SINUS TACHYCARDIA*

The heart rate varies markedly in different mammals In the elephant for example it is about 30 beats per minute in the rat it is close on 600 It is considerably slower in the hare than in the rabbit On the whole the speed is inversely proportional both to the size and to the athletic endurance of the animal In man the average heart rate is 72 beats per minute but there are wide limits of normality ranging between 40 and 100 The pulse is faster in children averaging 120 to 130 at birth and slowing gradually during childhood to reach about 80 at puberty The more athletic the individual the slower the pulse as a rule and in well trained athletes resting figures of 45 to 50 are common It follows that tachycardia may mean a heart rate faster than average faster than the upper limit of normality or faster than what is known to be normal for a particular individual

*Applied physiology* Tachycardia has always played an impressive part as a physical sign in general medicine It has received weighty consideration in fevers in all forms of heart disease in shock and hæmorrhage in various chronic diseases such as pulmonary tuberculosis and indeed in almost every condition yet it can mean little unless its immediate cause is under stood This is not to decry tachycardia as a valuable sign but to emphasise that its significance depends upon its mechanism

The speed of the sino atrial pace maker is strongly influenced by the autonomic nervous system Complete paralysis of the vagus may be produced within a minute by giving 2 to 3 mg of atropine sulphate intra venously whereupon the heart accelerates to a speed of 130 to 160 per minute The cardiac output per minute rises simultaneously but the fall in venous filling pressure that accompanies the tachycardia may counteract this effect (McMichael and Sharpey Schafer 1944) The ventricular stroke volume is diminished even in those with higher outputs Emotional tachy cardia as in the anxiety states and the tachycardia of convalescence appear to be due to diminished vagal tone

Tachycardia may be due to a rise in pressure within the great veins and right atrium venous receptors initiating the Bainbridge reflex by which vagal tone is reduced Under these circumstances the stroke-volume may be maintained or increa ed the cardiac output per minute rising in pro portion to the tachycardia or even higher This mechanism operates during effort and in anæmia beri beri arteriovenous shunt anoxic pulmonary heart disease generalised active Paget s disease and pregnancy The Bai bridge reflex is also partly responsible for the tachycardia so freq seen in congestive failure

The speed of the heart is also controlled by reflexes initiated by baro receptors in the aorta and carotid sinuses When the blood pressure rises vagal tone is increased and the heart slows when it falls vagal tone is diminished and the heart quickens (Marey s Law). This is the mechanism of the bradycardia associated with conditions causing a transient rise of blood pressure such as acute nephritis and it is part of the mechanism controlling the tachycardia of low blood pressure states

Anoxia may cause tachycardia by direct action on the central nuclei or possibly reflexly through the carotid sinus Just what part it plays in the production of tachycardia in anæmia and cor pulmonale is uncertain Thyroxin and fever have a direct stimulating action on the pace maker and so has adrenaline, but the latter may also excite the carotid sinus slowing reflex by raising the blood pressure so that the heart rate may change but little The elevated cardiac output that accompanies the tachycardia is also probably due in part to a direct action on the heart In the case of adrenaline the cardiac output may rise when there is no change in heart rate or blood pressure (McMichael and Sharpey Schafer 1944)

*Differential diagnosis* From the clinical point of view sinus tachycardia must be distinguished from auricular flutter and from paroxysmal tachy cardia This is usually possible at the bedside Sinus tachycardia varies in rate from minute to minute, or at least from hour to hour and it varies with emotion effort and change of posture Carotid sinus or eyeball com pression and release result in gradual rather than abrupt slowing and *quickening of the pulse respectively although changes may be difficult to* detect with fast rates In auricular flutter (and sometimes in paroxysmal auricular tachycardia) the rate is usually fixed neither varying spon

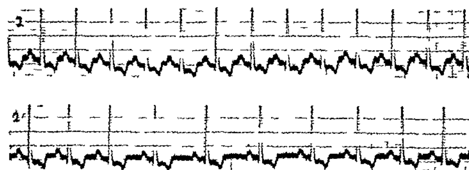


Fig 6 03—Sinus tachycardia slowed by carotid sinus compression

*taneously nor with emotion, effort, or change of posture* whilst on carotid sinus pressure slowing is abrupt often to half the rate 2 1 physiological atrio ventricular block being converted into a 4 1 relationship and on release reversion to the original rhythm is again abrupt and may not take place for several seconds Even without so precise a clinical analysis, the

degree of slowing may yet be too gross for sinus tachycardia In paroxysmal nodal and ventricular tachycardia the rate is also fixed, and carotid sinus pressure either stops the attack abruptly as in 50 per cent of the nodal cases or has no effect whatever If it is impossible to interpret the results of carotid sinus pressure clinically the problem may be solved by combining the manœuvre with an electrocardiogram (fig 6 03) It should be explained that an electrocardiogram *per se* may not afford certain distinction between these three rhythms although lead $V_1$ or $CR_7$ greatly facilitates analysis

*Effect on the heart* Sinus tachycardia presents an important problem in relation to heart failure Is it a causal factor or merely a reflection of cardiac embarrassment? Or is it part of a compensatory adjustment beneficial under the circumstances? Such questions are difficult to answer directly but the presentation of some of the relevant facts may help to clarify the issue A normal heart tolerates any natural degree and duration of sinus tachycardia rates approaching 200 for example being common during violent exertion and persistent rates of 120 or so being endured for over 20 years in certain cases of Da Costa s syndrome without harmful results On the other hand diseased hearts frequently develop congestive failure with heart rates of 150 to 200 in auricular flutter or paroxysmal tachycardia the effect being attributed to overwork and fatigue resulting from insufficient diastolic rest The tachycardia of the hyperkinetic forms of cardiovascular disorder (thyrotoxicosis anæmia anoxic cor pulmonale beri beri arterio venous aneurysm and generalised Paget's disease) is part of the physiological mechanism maintaining a high cardiac output and therefore performs a useful function but when the heart fails i e when it is overloaded the cardiac output falls and the tachycardia is wasted Under such circumstances tachycardia reflects cardiac embarrassment and deprives the heart of diastolic rest In the hypokinetic forms of heart failure such as those which may be seen in cases of hypertension and mitral stenosis tachycardia due to the Bainbridge or carotid sinus reflex is a reflection of cardiac distress from the start and serves no useful purpose In chronic constrictive pericarditis and to a lesser extent in high pressure pericardial effusion tachycardia may provide the only means of maintaining an adequate cardiac output for the stroke volume is strictly limited In the active forms of carditis (rheumatic diphtheritic and Fiedler s) and in bacterial endocarditis the heart rate may be disturbed by local pathology fever, toxæmia or (in diphtheria) by circulatory collapse and probably adversely affects the heart On the whole it may be said that the heart tolerates sinus tachycardia which tends to deprive it of rest better than a high cardiac output and much better than a raised blood pressure both of which increase its work

There is no treatment for sinus tachycardia itself but attention should be paid to its cause

*SINUS BRADYCARDIA*

As already stated, heart rates of 45 to 50 per minute are common in athletes Some individuals irrespective of their physical training have a naturally slow pulse Sinus bradycardia is a feature of certain diseases, notably myxœdema and obstructive jaundice and is not uncommon during convalescence from certain fevers especially influenza It also occurs when the blood pressure is raised rather suddenly as in acute nephritis the slowing being reflex through the sino aortic afferents and vagus It is a familiar sign of lesions that increase the intracranial pressure when it may be due to direct stimulation of central nuclei Slowing of the pulse may be induced temporarily by carotid sinus or eyeball pressure as a transient event it occurs naturally in vaso vagal syncope

The differential diagnosis between sinus bradycardia sino atrial block, and heart block can usually be made at the bedside but electro cardiographic confirmation is advised In sinus bradycardia the pulse quickens gradually with effort atropine, or amyl nitrite, in sino atrial block and sometimes in 2 1 heart block the rate doubles abruptly, whilst in complete heart block the degree of acceleration is barely perceptible Heart block may also be recognised by studying jugular pulsation and heart sounds (q v )

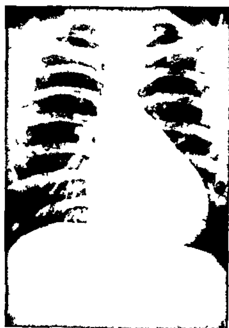


Fig 6 04—Relative cardiac enlargement due to sinus bradycardia

One of the consequences of sinus bradycardia is an increased ventricular stroke volume of sufficient degree to maintain a normal cardiac output per minute When the heart rate is 40 the stroke volume approaches double the average normal the diastolic heart size is larger than usual (fig 6 04) and in time hypertrophy may occur Such enlargement is physiological

When the speed of the pace maker approaches 40 per minute it may become slower than the natural speed of impulse formation in the atrio ventricular node in which event nodal rhythm occurs As sinus arrhythmia is often associated with bradycardia it is more usual to see irregular examples of ventricular escape the A V node taking over whenever a pause is un usually long (fig 6 05) Nodal rhythm would supervene more frequently if the influences that retarded the sinus node did not also depress the A V node

Sinus bradycardia is often associated with sinus arrhythmia sometimes with auricular ectopic beats and rarely with paroxysmal auricular fibrillation or flutter in elderly subjects Vagal influences appear to be responsible

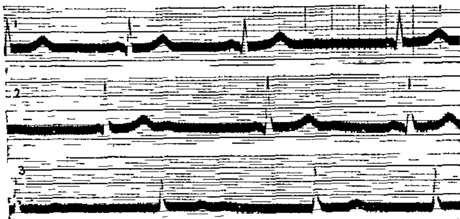



Fig 6 05—Nodal escape in sinus bradycard a

## *SINO ATRIAL BLOCK*

There are three types of sino-atrial-block corresponding to similar varieties of A V block First beats may be dropped irregularly the pauses being roughly equal to two normal intervals (fig 6 06) like the dropped beats of partial A-V block with fixed prolonged P R interval Second beats may be dropped more or less regularly the pauses being always less than two normal intervals like partial A V block with progressive lengthening of the P R interval until conduction fails – the Wenckebach type Third there may be 2 1 sino atrial block every second beat being dropped this gives rise to a slow regular heart rate which doubles on effort or with atropine (fig 6 07) It should be understood that there is no electrocardio graphic representation of the formation and discharge of the excitatory

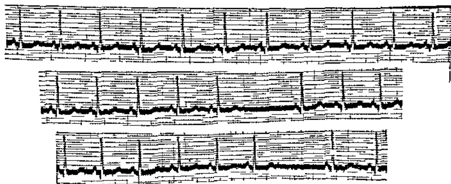


Fig 6 06—S no t ial blo k sho ng irregular dropped beats

impulse at the sinus node the first wave (P) of the electrocardiogram recording the passage of the impulse through the atria so that failure of conduction between the S A node and the atria can only be inferred

Sino atrial block is usually encountered in normal individuals, the first two types being commonly associated with sinus bradycardia It is a manifestation of increased vagal tone and may be abolished with atropine When there is 2 1 block and a pulse rate of about 40 per minute fluoroscopy may reveal cardiac enlargement due to the large stroke volume

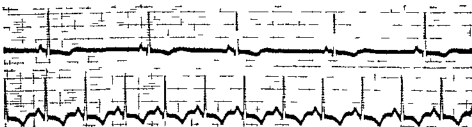


Fig 6 07—Sino atrial block the rate doubles on effort

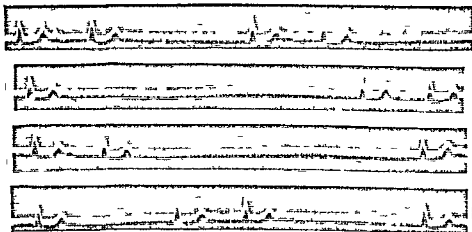


Fig 6 08—Cardiac standstill occurring spontaneously in sino atrial block
(By c t sy f D Raymond D ley)

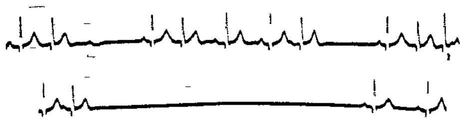


Fig 6 09—Cardiac standstill due to carotid sinus compression

necessary to maintain a normal cardiac output As with sinus bradycardia ventricular escape may occur and would probably be more common if the A V node were not also depressed

There are no symptoms of sino atrial block *per se* but occasionally short periods of cardiac standstill with dizziness or syncope may occur and appear to be due to bursts of extreme vagal activity (fig 6 08) They may be prevented by atropine Attacks of this kind may be readily induced in susceptible individuals by carotid sinus pressure (fig 6 09)

## *NODAL RHYTHM*

The sinus node is the pace maker of the heart only because its inherent rate of impulse formation and discharge is quicker than that of any other focus endowed with a similar property but if it is sufficiently depressed as by cooling some other focus may form its impulses at a faster rate and so become the temporary pace maker, and in fact this function usually falls upon the atrio ventricular node Under such circumstances atrial excitation is retrograde and the electrocardiogram usually shows an inverted (or deformed) P wave just after the QRS complex and a heart rate of 40 to 60 per minute (fig 6 10a) Sometimes however the P wave may precede (fig 6 10b) or coincide with the QRS complex or it may be absent altogether owing to retrograde block (fig 6 10c) Occasionally it may shift its position from moment to moment (shifting or sliding nodal rhythm, fig 6 11) if such graphs are examined critically however they are seen to be examples of sinus bradycardia with normally formed P waves and frequent ventricular escape (so called wandering or shifting pace maker) This terminology is misleading for a wandering pace maker is simply dual rhythm both S A and A V nodes discharging spontaneously with variable asynchronism

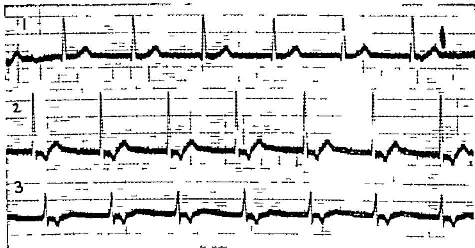
Clinically nodal rhythm may be recognised by its effect on the jugular venous pulse for whenever the right atrium contracts against a closed tricuspid valve sharp cannon waves occur (fig 6 12)

Nodal rhythm may be discovered by chance in healthy individuals it may occur in active rheumatic diphtheritic, and Fiedler s carditis, it may be momentarily induced by carotid sinus pressure and it may follow thrombosis of the right coronary artery above the origin of the branch to the sinus node (this branch arises from the left coronary artery in 40 per cent of cases) but its only common cause is digitalis therapy

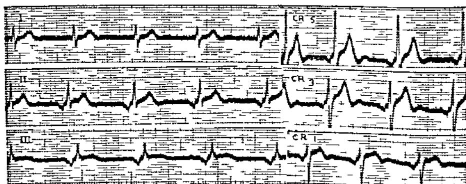
Nodal rhythm is under autonomic control the heart rate being slowed by vagal stimulation and accelerated by atropine and exercise (White 1915) It is a harmless rhythm change gives rise to no symptoms and requires no treatment When due to digitalis, there is no need to stop the drug

### *Coronary sinus rhythm*

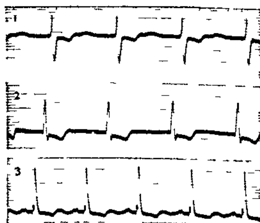
The position of the P wave in relation to QRS depends chiefly on the exact site of the pace maker in the A V node when situated in the proximal




(a) An inverted P wave occurs after QRS




(b) An inverted P wave precedes QRS ( Coronary sinus rhythm )




(c)—The P wave is invisible possibly buried in QRS (leads 1 and 2 lead 3 shows normal rhythm)

Fig 6 10—Nodal rhythm

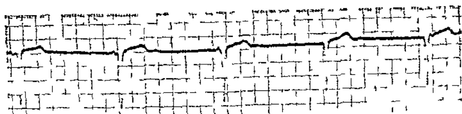


Fig 6 11—Asynchronous dual rhythm

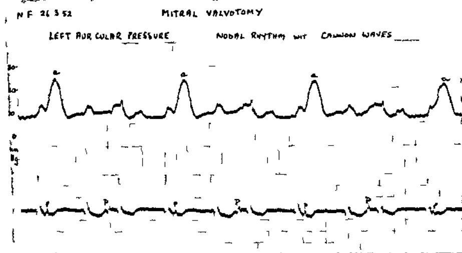



Fig 6 12 (a)—Nodal rhythm with partial retrograde block (Wenckebach type) showing reciprocal beats when the RP interval is sufficiently prolonged and cannon waves in the left atrial pressure pulse whenever the atria contract during ventricular systole

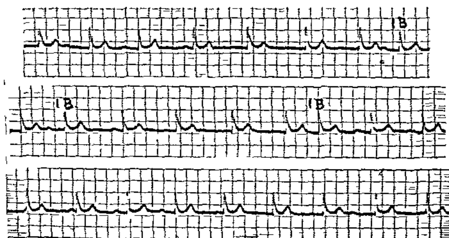



Fig 6 12 (b)—Interference dissociation The interference beats are labelled I B

or coronary sinus position of the node the pace maker is functionally nearer the atria than the ventricles and P falls just before QRS (fig 6 10b) This is called coronary sinus rhythm and is the most innocent and common type of nodal rhythm The P wave is nearly always inverted in standard leads II and III In view of the short P R interval the first heart sound may be accentuated

## RECIPROCAL RHYTHM

When retrograde conduction to the atria is delayed in nodal rhythm the R P interval may exceed 0 2 second by then the ventricles may be no longer refractory and may be re activated by a return of the excitation wave from the atria so that a *reciprocal* beat as it is called follows the P wave A form of coupling known as *reciprocal rhythm* may be brought about in this way each pair of ventricular beats having an abnormal P wave between them (White 1921) or if retrograde R P conduction shows progressive lengthening reciprocal beats may occur only at intervals when R P is sufficiently prolonged (fig 6 12a)

## INTERFERENCE DISSOCIATION

If retrograde conduction is completely blocked in nodal rhythm forward conduction remaining unimpaired *atrioventricular* dissociation occurs in which the ventricles beat faster than the atria the rate of discharge of the sinus node being necessarily slower than that of the A V node From time to time in such a rhythm atrial activation from the sinus node discharges the A V node prematurely and causes an *interference beat* the slightly irregular rhythm so produced being called *interference dissociation* (fig 6 12b)

# HEART BLOCK

When any organic lesion or functional disturbance impedes conduction through the bundle of His or through both its main branches we may speak of heart block There are four grades prolonged P R interval dropped beats partial block with fixed atrio ventricular relationship and complete heart block

## PROLONGED P R INTERVAL

As discussed elsewhere the upper limit of the normal P R interval should not exceed 0 22 second In partial heart block it frequently measures 0 28 to 0 32 second In extreme cases or when there is associated tachycardia electrocardiograms may show P coinciding with or even preceding the previous T wave (fig 6 13)

Prolongation of the P R interval may be transient or permanent or it may develop into a higher grade of block As a transient phenomenon it is especially characteristic of any form of active carditis but it may also be due to digitalis to coronary thrombosis, or to temporary nutritional

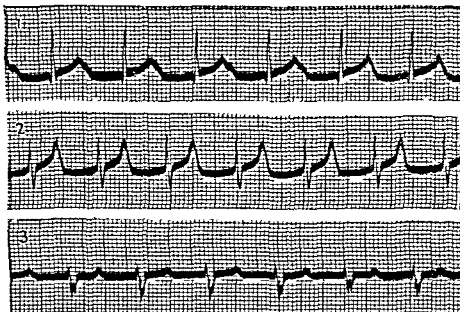



Fig 6 13—Prolonged P R interval with P coinciding with the previous T wave

changes from other causes and it may be induced by carotid sinus pressure Permanent delay in conduction may result from an inflammatory scar involving the bundle of His as in old rheumatic heart disease or from ischæmic fibrosis When the block is not permanent it may be relieved immediately by the intravenous injection of 1 to 3 mg of atropine sulphate (Bruenn 1937) A prolonged P R interval may also be shortened when the subject stands upright (Scherf and Dix 1952)

Although partial heart block of this kind is usually an electrocardiographic diagnosis it may be recognised clinically by noting delay between

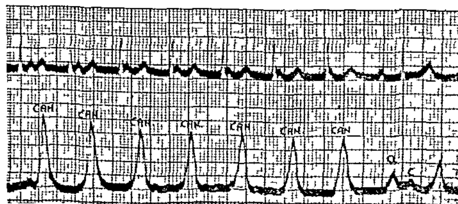



Fig 6 14—Partial heart block showing jugular cannon waves

the atrial and ventricular components of cervical venous pulsation or presystolic gallop rhythm by observing a gap between a presystolic murmur and the first heart sound in cases with mitral stenosis by hearing an unusually faint first heart sound or by detecting cannon waves in the neck when the P R interval is so prolonged that P falls between QRS and T in the previous cycle (fig 6 14) Its practical importance lies in its value as a sign of active rheumatic carditis

## *PARTIAL HEART BLOCK WITH DROPPED BEATS*

In a slightly higher grade of partial heart block, conduction through the bundle of His fails altogether from time to time so that ventricular beats are dropped In the type first recognised by Wenckebach (1899) the P R interval shortens considerably after a beat is dropped but subsequently lengthens progressively from cycle to cycle until conduction again fails (fig 6 15) In another type (Hay 1906) the P R interval is fixed and beats are dropped irregularly and unpredictably

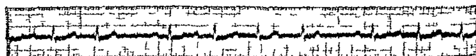


Fig 6 15—Partial heart block with dropped beats (Wenckebach type)

The condition may be detected clinically by noting a changing a c interval in the neck variations in the intensity of the first heart sound, and occasional cannon waves (fig 6 14) It is commonly transient and recovers spontaneously but occasionally progresses to complete heart block

## *PARTIAL HEART BLOCK WITH FIXED A V RELATIONSHIP*

Relatively stable forms of partial heart block may be encountered, usually with a 2 1 atrio ventricular relationship (fig 6 16) but occasionally with

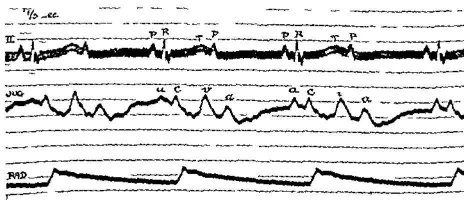



Fig 6 16—2–1 heart block
(By courtesy of Sir John Parkinson)

3 1 or even 4 1 A V ratios These usually progress to complete heart block they are much less common in active carditis than in ischæmic cases

Clinically 2 1 heart block has to be distinguished from sino atrial block from sinus bradycardia with a heart rate of about 40 beats per minute from nodal rhythm and from complete A V dissociation Failure to quicken appreciably with effort or atropine excludes sino atrial block and sinus bradycardia (and usually nodal rhythm) The absence of both irregular cannon waves and varying intensity of the first heart sound distinguish it from complete heart block

## *COMPLETE HEART BLOCK*

*Etiology* Complete atrio ventricular dissociation is very rare in active rheumatic carditis but less so in diphtheritic carditis it may be induced by digitalis especially in cases of auricular fibrillation and has been caused by hæmorrhage into the bundle of His from trauma or asphyxia and by primary or secondary neoplasm About 10 per cent of cases are congenital (q v) As a rule however complete heart block is associated with ischæmic or hypertensive heart disease with syphilitic aortitis or with extensive calcification of the aortic cusps or mitral ring in elderly atherosclerotic subjects and is due to a fibrotic or calcified lesion in the bundle of His or in both its main branches Occasionally no cause can be found

*Clinical features* Complete A V dissociation is four times more common in males than in females and 84 per cent of cases occur in patients over 50 years of age (Campbell 1944) It is usually permanent but under special circumstances may be transient or even paroxysmal (Lawrence and Forbes 1944) It is characterised by an extremely slow heart rate a water hammer or collapsing pulse elevation of the venous pressure cervical venous pulsation unrelated to ventricular contraction audible independent atrial sounds the occurrence of cannon waves in the neck and varying intensity of the first heart sound general enlargement of the heart and syncopal attacks of a special kind It is proved electrocardiographically (fig 6 17)




Fig 6 17—Complete heart block Ventricular rate 18 beats per minute

Whilst the pulse rate is usually about 28 to 36 beats per minute based on the inherent rate of impulse formation of the idio ventricular pace maker distal to the block in the bundle of His it may be so slow as to induce a state of continual faintness (fig 6 18) as in the case originally described by Spens (1793) in which it fell to 9 beats per minute At the other extreme complete A-V dissociation may be seen with a ventricular rate of over 100 the ventricles sometimes beating more rapidly than the atria (fig 6 19)

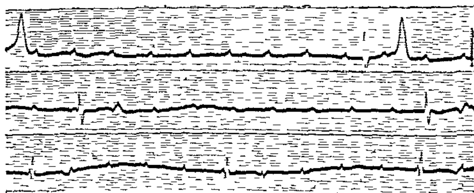


Fig 6 18—Complete heart block Ventricular rate 10 beats per minute

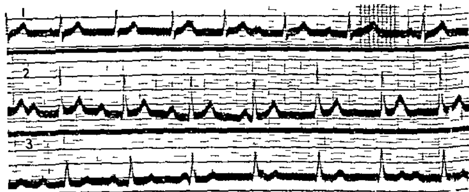



Fig 6 19—Complete A V dissociation with the ventricles beating faster than the atria

On the whole rates are faster when QRS is normal in width slower when the QRS resembles left or right bundle branch block (Kay 1948) Idio ventricular pace makers are little affected by stimuli that influence the S A and A V nodes so that the pulse rate usually remains remarkably constant in complete heart block In transient or paroxysmal cases however in which a functional element may be present temporary restoration of sinus rhythm may accompany fever as in the case described by Gerbezius in 1719 (Major, 1932)

A high systolic blood pressure is usual and is due to the large ventricular stroke volume Owing to associated vasodilatation however the pressure is not well maintained but tends to fall away rapidly in diastole giving rise to a collapsing pulse and to a rather low diastolic blood pressure

Under favourable circumstances inspection of cervical venous pulsation may reveal atrial waves (*a* waves) *independent* of ventricular events (*c* and *v* waves) as noted by Stokes (1846) Simultaneously may be heard the faint sounds of isolated atrial contractions (the semi beats of Stokes) either at the apex beat or down the left border of the sternum

Venous cannon waves occur when the P wave falls between QRS and T i e when the right atrium contracts against a closed tricuspid valve and are easily recognised by their abrupt quality high amplitude and variability Changing intensity of the first heart sound is equally characteristic the loudest sounds are heard when the P R interval is around 0 10 to 0 12 second left atrial contraction then forcing the mitral cusps wide open just before ventricular systole (Levine 1948) When the atria contract during *the period of rapid ventricular filling a loud third sound or short functional* mitral diastolic murmur may be heard the variability of this summation effect from beat to beat is as characteristic of complete heart block as the varying intensity of the first heart sound

Cardiac enlargement is usually more conspicuous than that seen in sino atrial block or in sinus bradycardia but is of the same quality unless the size and shape of the heart are altered by other effects of the underlying disease process

The cardiac output can only be maintained by a large stroke volume propelled with great force Diastolic distension is favoured by a compensatory rise in venous pressure and this must be very considerable during effort The early development of congestive failure is readily understood

*Stokes Adams attacks* Syncope due to ventricular asystole (Stokes Adams attacks) occurs in about 50 per cent of cases and is especially common when partial block becomes complete Loss of consciousness is abrupt without warning If standing the patient collapses and lies limp still pale and pulseless with fixed dilated pupils – as if dead breathing however continues If the attack lasts long enough i e for more than 10 seconds or so twitchings commence and may progress to convulsions and if ventricular asystole continues for more than 2 or 3 minutes recovery is rare As a rule however ventricular beating is resumed after a few seconds consciousness returns abruptly and a vivid flush ensues When an attack occurs in bed the lack of warning short duration of unconsciousness and abrupt return of full possession of the faculties may prevent a dull patient from being aware of the fit and he may only notice the flush The sequence of events both symptomatically and objectively is so characteristic as to make the diagnosis probable on the history alone – a point of some importance in patients with paroxysmal block who may present themselves with

normal sinus rhythm. In such … pressure may provoke an attack or induce paroxysmal …

Physiologically Stokes-Adams … to depression of a … tial or established idioventr… in cases of complete heart

Fig. … —Stokes-Adams … and sinus pressure in a patient with paroxysmal … heart block

block the ventricles stand still while the atria continue to beat. They are apt to occur when *partial block* becomes complete either because such an event is usually associated with some depressive influence on conduction which may … depress ventricular pace makers (even though considered beyond vagal control) or because idioventricular pace-makers are by nature initially sluggish. When complete block is well established attacks may still occur but are less common. The abrupt loss of consciousness depends upon sudden total failure of cardiac output. Twitching is due to cerebral anoxia and is not seen in short attacks. Convulsions are of two types, one being an exaggeration of anoxic twitching, the other occurring after restoration of ventricular action and synchronising with the flush (*Formijne* 1938). In the second type convulsions and flushing appear to be due to carbon dioxide depletion in the blood stagnant in the lungs during the phase of asystole with continued respiration and to vasodilatation resulting from accumulation of tissue metabolites so that when ventricular beating is resumed, blood rich in oxygen but containing practically no carbon dioxide is thrown abruptly into a widely dilated vascular bed. More often a period of apnœa follows the attack with or without subsequent Cheyne Stokes breathing (Griffith 1931). Apnœa of course may also occur towards the end of long periods of ventricular asystole when it is due to failure of the respiratory centre resulting from profound cerebral anoxia.

An important complication of Stokes-Adams attacks is paroxysmal ventricular tachycardia or fibrillation (Parkinson, Papp and Evans 1941). In

such cases it may be impossible to determine clinically whether unconsciousness is due to asystole or to ventricular fibrillation It is probable that many deaths are due to the supervention of such rhythm changes rather than to asystole

*Prognosis* Congenital and transient cases do relatively well unless the disease responsible is serious for other reasons The outlook in paroxysmal and acquired permanent cases however is poor life expectancy averaging 4½ years (Graybiel and White 1936 Campbell 1944) Those with a history of Stokes Adams fits have a much worse prognosis than those without the majority of them dying suddenly Those without fits usually die from congestive heart failure

*Treatment* The most effective prophylactic treatment for faintness or syncope is the oral administration of ephedrine ½ grain (32 mg) t d s If attacks are frequent and the patient bedridden adrenalin, 0 5 mg (8 minims or 0 5 ml of a 1 1 000 solution) should be injected subcutaneously and repeated every two to six hours Sublingual isoprenaline 20 mg is also helpful (Nathanson and Miller 1949) but noradrenalin has very little stimulating action on ventricular rhythm (Nathanson and Miller 1950) Both ephedrine and adrenalin prevent undue depression of the ventricular pace maker and encourage the heart to beat a trifle faster It is sometimes said that idio ventricular rhythm cannot be influenced by any of the drugs or manœuvres that are known to affect the sinus node This is not always strictly true but changes are admittedly slight Effort for example may quicken the ventricular rate in complete heart block the adrenergic drug fever and even atropine may also do so In treatment however atropine is valueless alone although it may enhance the effect of adrenaline Barium chloride had a vogue its action depending upon its power to excite ventricular ectopic beats and so to prevent ventricular standstill but this is a poor substitute for the physiological benefit provided by ephedrine In paroxysmal cases when some functional disturbance must be postulated inhalations of amyl nitrite may abort attacks (Lawrence and Forbes 1944)

A problem arises when repeated seizures are partly due to paroxysmal ventricular tachycardia or fibrillation for if it is uncertain whether unconsciousness is due to asystole or to fibrillation the administration of adrenaline may be hazardous since the drug encourages the latter rhythm change If paroxysmal ventricular tachycardia is demonstrated neither quinidine nor procaine amide should be given for both depress conduction and may cause ventricular standstill (Miller *et al* 1952 Schwartz *et al* 1952 1953) Sublingual isoprenaline 20 mg has been recommended in these cases (Schumacher and Schmock 1954)

Very slow heart rates may be accelerated by means of intravenous infusions of sodium lactate in doses of 5 to 15 ml per minute of a molar (11 2 G per 100 ml) or half molar solution (Bellet Wesserman and Brody 1955) Lactate may serve as a myocardial fuel or the rise in pH (increased blood bicarbonate) that results from the treatment may accelerate the heart

Treatment of the primary cardiac condition may help This applies especially to the rare transient cases associated with active carditis or myocardial infarction and to permanent cases associated with syphilitic aortitis. Very rarely a small gumma may interrupt the conducting pathway, and the resulting block may be cured with iodides (Major, 1923)

If congestive heart failure calls for digitalis therapy the drug should not be withheld on account of coincident heart block but should be adminis tered with caution Massive and intravenous doses should be avoided but digitalis leaf 3 grains (0 2 G) t d s on the first day 2 grains (0 13 G) t d s on the second and 1 grain (65 mg) thereafter twice daily is usually safe Should a Stokes Adams fit appear to be provoked the drug must be dis continued

In special clinics external electrical pace makers may be available to tide a heart over a critical period The machine is designed to deliver an elec trical shock of 75 to 150 milliamps at 45 to 100 volts for two to three milliseconds 60 to 90 times per minute the negative electrode is placed over the region of the apex beat the positive on the opposite side of the chest posteriorly (Zoll Linenthal and Norman 1954)

## BUNDLE BRANCH BLOCK

Although bundle branch block is not strictly a disorder of rhythm it may be discussed here conveniently on account of its close pathological relationship to other forms of conduction defect

*Anatomy* Bundle branch block occurs when some organic lesion inter feres with conduction through one or other of the two main branches of the bundle of His As may be seen from figure 6 01 the main bundle after piercing the membranous septum divides into two, one branch passing down each side of the muscular interventricular septum just beneath the endocardium and spreading out fan wise distally the left branch may sub divide into anterior and posterior divisions in the lower half of the septum (Mahaim 1931) The A V node bundle of His and posterior division of the left bundle branch receive their blood supply from perforating septal arteries arising from the posterior descending branch of the right coronary artery, the right bundle branch and the anterior division of the left are supplied by perforating septal branches of the left anterior descending coronary artery (Gross 1921) Considerable variations occur, however, especially as vital reactions to ischæmia

*Nomenclature* When the left bundle branch is interrupted the excitatory process reaches the right ventricle first through the relatively normal right bundle branch and spreads throughout that chamber before passing across to the left The right ventricle therefore contracts first The electrocardio gram described and illustrated in Chapter III shows a wide QRS com plex measuring from 0 11 to 0 18 second the main deflection of which is usually upright in lead 1 and downward in lead 3, with marked slurring or notching and followed by a conspicuous T wave usually in the opposite

direction Right bundle branch block (Wilson *et al* 1934) is characterised by widening of the initial ventricular deflection to 0 11 to 0 14 second by late slurring of QRS – usually best seen in $S_1$ – and by an upright T wave in lead 1 That the first type of graph described represents left bundle branch block has been proved by the reconstructed vectorcardiograms (monocardiograms) of Mann (1931) by the electrocardiographic discoveries of Wilson and his colleagues (1932) by kymographic and polygraphic studies revealing delayed left ventricular events (Wolferth and Margolies 1935) by experiments on revived human hearts in normal position in which one or other bundle branch has been cut (Kountz 1936) and by simultaneous electrocardiographic phonocardiographic and polygraphic records demonstrating and analysing ventricular asynchronism (Braun Menendez and Solari 1939) The detailed histological work of Mahaim (1931) which at first appeared to support the original view in which the nomenclature for left and right bundle branch block was reversed has been ably reviewed by Yater (1938) who presented extensive histopathological evidence of his own and concluded that the bilateral lesions invariably demonstrable rendered reliable interpretation difficult but that on the whole the findings supported the new terminology Finally the clinical facts cannot be disregarded left bundle branch block is commonly seen in lesions involving the left side of the heart whereas right bundle branch block is usually associated with enlargement of the right ventricle This general principle was recognised by Tung and Cheer (1933) and by Bayley (1934)

*Etiology* Left bundle branch block is usually due to hypertensive heart disease, ischæmic heart disease, or aortic valve disease right bundle branch block to mitral stenosis atrial septal defect or massive pulmonary embolism Either form may occur in active rheumatic diphtheritic or other form of carditis in any disease affecting the heart as a whole such as thyrotoxicosis and fibrosis of the myocardium of known or unknown etiology and as a result of any local lesion such as neoplasm Partial forms are common and tend to progress on the other hand both left and right bundle branch block may be transient paroxysmal or even alternating (fig 6 21) sometimes in association with paroxysmal tachycardia auricular flutter or fibrillation sometimes during an episode such as acute myocardial infarction congestive heart failure or massive pulmonary embolism but also spontaneously Right bundle branch block is sometimes found in otherwise healthy individuals even in youth left bundle branch block very rarely so

*Clinical features* Clinically left bundle branch block may be suggested by presystolic gallop rhythm in the absence of ventricular distress and by reversed splitting of the second heart sound $A_2$ falling after $P_2$ so that the split closes on inspiration and widens on expiration Right bundle branch block is suggested by wide splitting of the second sound $P_2$ falling later than usual When the heart is enlarged and it is uncertain which chamber

is mainly involved the presence of left or right bundle branch block points strongly to the homolateral ventricle Left bundle branch block provides convincing proof of serious heart disease but right bundle branch block must be interpreted more cautiously Neither form is influenced by digitalis atropine, or by any of the adrenergic or cholinergic drugs




Fig 6 21 – Alternating left bundle branch block

*Prognosis* The average life expectancy for cases of bundle branch block in general has been estimated at 3 years (Campbell 1944) but it should be clearly understood that in any given patient the prognosis is that of the underlying heart disease and is not influenced by the conduction defect Again if right bundle branch block is found in an otherwise normal individual the outlook does not differ from normal controls (Wood Jeffers and Wolferth 1935)

## ECTOPIC BEATS

Ectopic beats are premature systoles induced by the discharge of some ectopic impulse forming focus situated anywhere in atrial nodal or ventricular tissue They are necessarily premature because all potential impulse forming foci are otherwise discharged by the excitation which reaches them from the sinus node

*Physiology In the atrial type* (fig 6 22) the P wave is abnormal in shape or direction according to the site of the ectopic focus and to the direction in which the impulse flows over the atria In these cases the partially charged sinus node is discharged when the impulse reaches it so that the compensatory pause following the ectopic beat is slight being equal to a normal cycle plus the interval between the onset of the ectopic and the

arrival of the retrograde excitatory process at the S A node The timing of the heart beat is permanently altered The ventricular complex is usually normal but may be slightly deformed as a result of a functional defect in conduction If an atrial ectopic beat is very premature it may be blocked altogether




Fig 6 2 —Atrial ectopic beats

*Nodal ectopic beats* (fig 6 23) are premature beats arising in any part of the atrio ventricular junctional tissue The QRS complex is normal or slightly deformed as described above but the P wave is inverted and occurs just before during or just after the QRS complex according to the more proximal or more distal site of the ectopic focus and to the degree of resistance opposed to retrograde conduction Discharge of the sinus node (unless there is retrograde block) again prevents a full compensatory pause

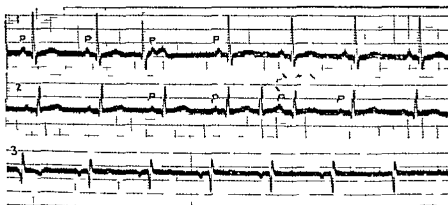



Fig 6 23—Nodal ectopic beats Slight deformity of QRS is due to fatigue block In I the P wave immediately after the ectopic is blocked In lead 2 the nodal ectopic is interpolated In both there is retrograde block

*Ventricular ectopic beats* are characterised by a full compensatory pause for the sinus node is not discharged by the premature impulse owing to retrograde block (physiological) in the bundle of His or to natural delay in retrograde conduction and so continues to function at its usual time Its first discharge after the ectopic however is blocked by the refractory state of the ventricles and so there is a pause until its second discharge The final timing of the heart beat therefore remains unchanged Electrocardiographically a ventricular ectopic beat resembles a bundle branch block

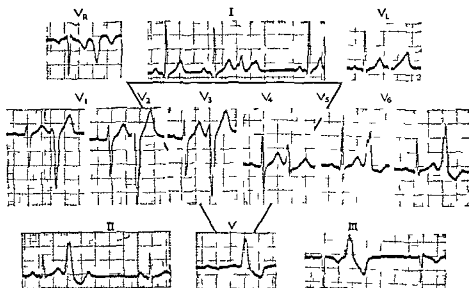



Fig 6 24—Right ventricular ectopic beats

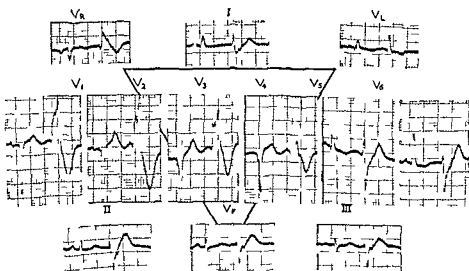



Fig 6 25—*Left ventricular ectopic beats causing coupling*

complex QRS being widened and notched and T being prominent and usually in the opposite direction When the deflection is like left bundle branch block the ectopic focus lies in the right ventricle (fig 6 24) when QRS is like right bundle branch block, the ectopic focus lies in the left ventricle (fig 6 25) There are many variations however depending upon the exact site of the irritable focus (Barker *et al* 1930 Kountz 1936) Ventricular ectopic beats may also be interpolated (fig 6 26)



Fig 6 26—Interpolated ventricular ectopic beats

Premature beats have a smaller stroke volume than normal and if very premature may not be perceptible at the wrist or audible with a stetho scope The beat that follows is fuller than usual and is appreciated by the patient as a hard thump This is a matter of cardiac filling the earlier the ectopic beat the emptier the heart the longer the compensatory pause, the fuller the heart The blood pressure varies directly with the stroke output

*Clinical diagnosis* Clinically ectopic beats must be distinguished from other irregularities especially from auricular fibrillation and from partial heart block with dropped beats Whilst this may be easy in the majority of cases confusion arises with multiple atrial ectopic beats which may be indistinguishable from auricular fibrillation and with inaudible imper ceptible or blocked ectopic beats which mimic partial heart block with dropped beats Alternate ectopic beats or coupled beats may be confused with S A block when very premature with a dicrotic or bisferiens pulse or even with pulsus alternans If there is any doubt the effect of effort amyl nitrite or of 1 mg of atropine sulphate should be determined ectopic beats usually disappear as the heart quickens, and may be exaggerated as it slows down again Ectopic beats often cause cannon waves in the neck whereas auricular fibrillation cannot do so

*Etiology* Experimentally ectopic beats may be produced by electrical stimulation of any part of the heart Certain drugs notably digitalis bari chloride and adrenaline may produce them Excessive use of tob

occasionally seems responsible. They are common in pregnancy. Whilst almost any state of ill health may be blamed for their occurrence no common factor has been discovered and in the majority of cases there is no evidence of structural disease of the cardiovascular or other systems. Occasionally, however, atrial ectopic beats may herald auricular fibrillation, especially in mitral stenosis and thyrotoxicosis. Under certain circumstances also ectopic beats are probably due to organic disease, for example, their occurrence during the course of diphtheria may be due to toxic carditis, but as innocent ectopic beats are common enough after simple streptococcal tonsillitis and indeed during convalescence from any fever, it is impossible to draw any conclusion from their presence. Again, ectopic beats following coronary thrombosis are probably significant and to be explained by irritable foci set up by ischæmia, but are equally common in conditions that may simulate myocardial infarction. On the whole, *therefore*, it is wise to assume the innocence of ectopic beats under any conditions and to judge organic disease on other grounds.

*Treatment.* Many patients are unaware of premature systoles, others may seek relief from palpitations. Treatment includes fresh air, exercise and a healthy physiological life. Of drugs, potassium bromide 10 grains (0·65 G.) t.d.s., phenobarbitone ½ grain (32 mg.) t.d.s., or quinidine 5 grains (0·32 G.) t.d.s. may prove effective. Alternate ectopic beats (coupling) due to digitalis provide good grounds for stopping the drug or reducing its dose. Potassium salts are efficient (Sampson and Anderson, 1932; Castleden, 1941), but the large dose usually required is not without danger of sudden death and may provoke symptoms as unpleasant as the palpitations, chiefly nausea and vomiting; the chloride or acetate is employed as a 10 to 20 per cent aqueous solution and may be given by mouth in safe doses of 2 to 4 G. three or four times a day. Larger doses are not advised. Pronestyl 0·25 to 0·5 G. four to six hourly by mouth usually abolishes ventricular ectopic beats. Reassurance is important and should be unconditional and convincing, for ectopic beats rarely constitute a complaint except in those prone to morbid anxiety.

## PARASYSTOLE

*Parasystolic rhythm* is said to occur when an ectopic focus releases an excitatory impulse at regular intervals independent of the pace maker. The ventricles respond to this impulse whenever it reaches them outside their refractory phase.

## PAROXYSMAL TACHYCARDIA

When ectopic beats occur in rapid and regular succession from the same focus one may speak of paroxysmal tachycardia. The name was introduced by Bouveret in 1889. The ectopic focus may be supraventricular (atrial or nodal) or ventricular. The electrocardiographic complexes in the three types are precisely the same as those in the three types of ectopic beat.

The patient usually complains of attacks of palpitations characterised by

the abruptness of their beginning and end by the rapidity and regularity of the beats and by the relative well being of the patient (Cotton 1867) Until an attack is witnessed the diagnosis rests upon an accurate history Experience shows that most careful cross examination is required to establish the true sequence of events It is not enough to determine that the onset is sudden it is necessary to be sure it is abrupt that the full velocity of the attack is reached immediately in the space of one beat that from no sensation whatever maximum palpitation develops within one second To assess the rate and rhythm it is helpful to ask the patient to represent them by tapping with his finger The manner in which the attack ends may be more difficult to establish some patients become accustomed to the palpitations and gradually fail to perceive them others pass from a true paroxysm to sinus tachycardia without appreciating the change and their description of the end refers to the gradual slowing down of the sinus rhythm

Attacks may last from a few seconds to several weeks but are usually measured in hours and rarely exceed three days The speed ranges between 110 and 250 beats per minute but is between 140 and 240 in 90 per cent of cases and between 150 and 200 in 50 per cent (Campbell 1947) Occasionally however much faster rates have been recorded For instance in one of Bouveret s cases the heart rate was 300 per minute If the heart is normal as it is in 62 per cent of the supraventricular variety, there is usually a remarkable degree of polyuria *during* the attack at least in cases with heart rates up to 180 beats per minute there are usually no other symptoms apart from those provoked by anxiety but if the attack is unduly prolonged or the heart rate exceptionally rapid congestive failure or angina pectoris may occur If the heart is abnormal however as it is in 80 per cent of the ventricular variety the rapid development of congestive heart failure is common With very rapid rates syncope may occur and in ischaemic heart disease status anginosus Physiologically, the effects depend upon the functional capacity of the heart to increase its output with tachycardia and on its ability to stand up to the extra work imposed with minimal rest In any given case there must be a critical rate above which the cardiac output falls

## *SUPRAVENTRICULAR PAROXYSMS*

As just indicated both paroxysmal atrial and nodal tachycardia are most commonly encountered in healthy individuals and have little more significance than ectopic beats or spontaneous fluttering of somatic muscle They are fifteen times more common than ventricular paroxysms When attacks occur in patients with heart disease the prognosis is not so good and depends upon the nature and severity of the cardiac lesion and the speed and duration of the paroxysm Even so the mortality rate is only about 1 per cent

A clinical diagnosis may be accepted if the spontaneous or in

beginning or end of an attack is proved to be abrupt if the heart rate during a paroxysm exceeds 150 per minute and does not vary with effort, change of posture atropine amyl nitrite carotid sinus (or eyeball) pressure prostigmine, or mecholin if any such measure terminates the paroxysm if the duration of attacks is a matter of hours rather than one of minutes days or weeks if the patient is relatively young i e under 40 years of age or was so when he had his first attack if paroxysms have continued with variable frequency for more than five years and if there is no evidence of organic heart disease or thyrotoxicosis Electrocardiographic proof however which may require a record of the beginning or end of an attack should be obtained whenever possible Although only a rare chance will enable the onset to be registered the end may be recorded in over half the cases by means of a continuous tracing while the attack is terminated by carotid sinus pressure or mecholin (fig 6 27) If the attack is not terminated such measures may yet serve to differentiate paroxysmal tachycardia from sinus tachycardia and from auricular flutter for in paroxysmal tachycardia the heart rate is rarely altered whereas in sinus tachycardia it is slowed and in auricular flutter it is often abruptly halved Occasionally however carotid sinus pressure may block paroxysmal atrial tachycardia (fig 6 28)

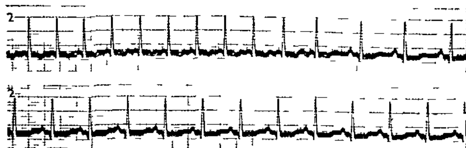



Fig 6 27—Paroxysmal atrial tachycardia terminated by means of mecholin

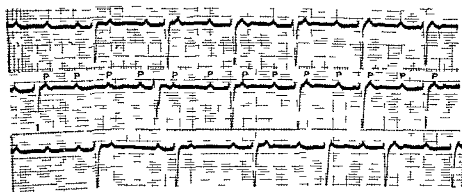



Fig 6 8—Paroxysmal atrial tachycardia blocked by carotid sinus compression

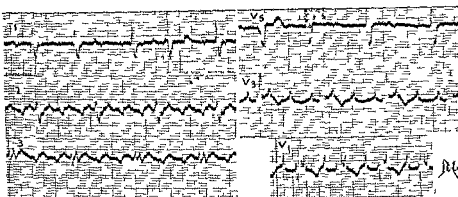



Fig 6 9—Paroxysmal atrial tachycardia showing varying degrees of spontaneous A V block




Fig 6 30—Paroxysmal atrial tachycardia slowed by means of quinidine

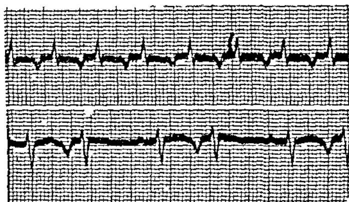


Fig 6 31—Paroxysmal atrial tachycardia followed by atrial ectopic beats

Evans (1944) first presented evidence based on lead CR1 suggesting that many cases that would ordinarily be interpreted as 2 : 1 atrial flutter might really be examples of paroxysmal atrial tachycardia with 2 : 1 A-V block, and that these two conditions were essentially the same. Certainly paroxysmal atrial tachycardia may show varying degrees of A-V block (figs. 6.28 and 6.29) and the atrial waves may be slowed by means of quinidine (fig. 6.30) in the same way as flutter; there is also no doubt that the same patient may show all varieties of atrial rhythm, suggesting that they all depend upon a similar mechanism, and that the occurrence of atrial ectopics before or after a major attack (fig. 6.31) offers an obvious clue as to their essential nature. Indeed, Prinzmetal (1950) has now provided convincing evidence not only of the unity of paroxysmal atrial tachycardia and flutter but also of atrial ectopic beats and auricular fibrillation, all four disturbances of rhythm depending upon the presence and behaviour of an ectopic irritable focus. Nevertheless, the clinical differences between paroxysmal tachycardia and flutter (not to mention auricular fibrillation and ectopic beats) are considerable (Campbell, 1945) and their separate identities should be preserved. Similarly, there can be no thought of not maintaining the separate identities of ventricular ectopics, ventricular tachycardia and ventricular fibrillation, yet all three must depend on a similar physiological mechanism.

## *PAROXYSMAL NODAL TACHYCARDIA*

Nodal paroxysms may be difficult to distinguish from atrial tachycardia when the rate is fast, unless the beginning of an attack can be recorded (fig. 6.32). At slower rates the electrocardiogram resembles fast nodal rhythm. Clinically, nodal tachycardia may often be recognised by the large regular cannon waves which dominate the jugular venous pulse (fig. 6.33).

Nodal tachycardia is commonly innocent and responds particularly well to carotid sinus pressure and cholinergic drugs.




Fig. 6.3 —Paroxysmal nodal tachycardia beginning with a nodal ectopic beat

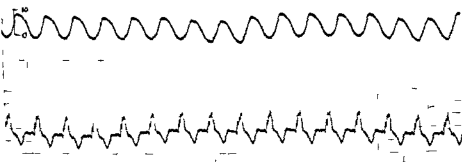


Fig 6 33—Paroxysmal nodal tachycardia showing regular cannon waves in the right atrial pressure pulse in a case of Ebstein s disease with right branch block

## VENTRICULAR PAROXYSMS

Paroxysmal ventricular tachycardia is relatively rare is usually associated with organic heart disease in patients between the ages of 40 and 70 and is twice as common in men as in women It tends to arise in a badly damaged heart as in heart failure from hypertension or from aortic valve disease it may follow myocardial infarction or succeed a Stokes Adams fit occasionally it is due to digitalis in about 20 per cent of cases it is innocent

It has the same clinical features as the supraventricular variety apart from the circumstances in which it occurs and its lack of response to carotid sinus pressure and cholinergic drugs, moreover, it is more frequently followed by congestive heart failure and sometimes by ventricular fibrillation and sudden death The prognosis is correspondingly grave

Ventricular tachycardia may be recognised at the bedside if there are

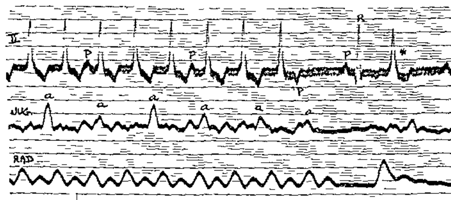



Fig 6 34—Paroxysmal ventricular tachycardia showing independent P waves at a slower rate Note the a wave and variable cannon waves in the jugular tracing

(B ... f S J Park ...)

occasional cannon waves in the jugular pulse or if the first heart sound is occasionally extra loud, for both these phenomena indicate a varying atrio ventricular relationship

Proof of the nature of the attack is obtained by electrocardiography (fig 6 34) but difficulty may arise when supraventricular paroxysms or auricular flutter are complicated by previously established or functional bundle

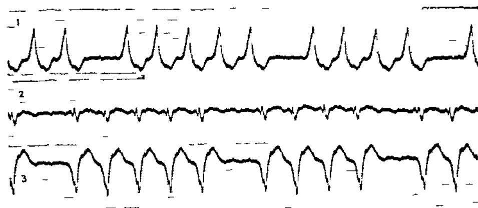
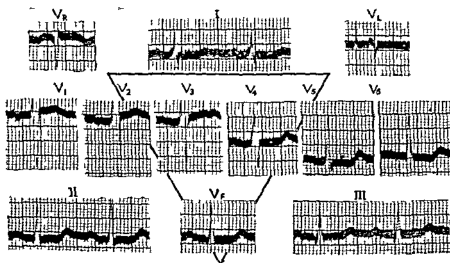



Fig 6 35—Auricular flutter with left bundle branch block

Fig 6 36—(a) During attack (rate 150)

(b) After resumption of normal rhythm showing inverted T waves over a wide area




(c) After normal rhythm has been maintained for three months

Fig 6 36—Serial electrocardiograms from a case of paroxysmal ventricular tachycardia



(a) Acute cardiac dilatation



(b) Normal heart shadow after resumption of normal rhythm and recovery from congestive failure

Fig 6 37—Heart failure in primary paroxysmal tachycardia

branch block (fig 6 35) The diagnosis is more certain if independent P waves can be made out at a much slower rate but even then nodal tachycardia with bundle branch block and retrograde A V block is possible

Gross heart failure from prolonged paroxysmal ventricular tachycardia does not necessarily signify organic heart disease When the rhythm is restored to normal widespread inversion of the T wave points to nutritional changes in the myocardium but these are always reversible if the rhythm change is primary (fig 6 36) Cardiac enlargement due to failure is also reversible (fig 6 37)

## *TREATMENT*

Supraventricular paroxysms *when of nodal origin* may be terminated by some mechanical trick already known to the patient such as holding the breath, by carotid sinus or eyeball pressure in about 50 per cent of cases and by the cholinergic drugs in 75 per cent Devices discovered by the patient include the adoption of some particular posture drinking iced water forced breathing or breath-holding compression of the abdomen and self induced vomiting

The carotid sinus is located at the bifurcation of the common carotid artery at the level of the superior border of the thyroid cartilage It should be firmly compressed for several seconds against the bodies of the cervical vertebræ by means of the observer s thumb first on one side then on the

other but never together Bilateral eyeball compression is also carried out with the thumbs should be sufficiently forceful to cause pain and should be maintained for 3 to 5 seconds A depressor response of the same kind may be elicited by stimulating the baroreceptors in both carotid sinuses and in the aortic bodies by injecting some pressor agent such as phenylephrine (neosynephrine) 0 25 to 0 5 mg intravenously (Youmans *et al* 1949)

Of the cholinergic drugs mecholin (acetyl beta methylcholine) is the most successful (Starr 1933) and prostigmine the least unpleasant in the doses employed doryl (carbo amino acetylcholine) is less effective and acetylcholine itself too drastic besides being technically difficult owing to its rapid destruction in the bloodstream Mecholin should be given intra muscularly or subcutaneously in a dose of 10 to 20 mg and may be expected to work in about five minutes prostigmine may be administered intravenously or intramuscularly in a dose of 1 to 2 mg and has its maxi mum effect in about half an hour Side effects include urgent micturition and defæcation colic vomiting sweating flushing and faintness but these are absent or slight with 1 to 1 5 mg of prostigmine and rarely severe with 10 mg of mecholin Should they prove too unpleasant and the object of the drug has not been achieved they may be abolished at once by injecting 1 to 2 mg of atropine sulphate intravenously but this is obviously not advised unless absolutely necessary Cholinergic drugs should not be given to patients who are prone to bronchial asthma for they may then excite violent bronchospasm

*Paroxysmal atrial tachycardia* does not usually respond to any of these measures the drug of choice in these cases being digitalis It was used originally to slow the ventricular rate by causing partial heart block as it does in flutter, and also to treat heart failure when that was present while these objects were being achieved normal rhythm was resumed so fre quently that digitalis had to be given the credit for that too For a quick response digoxin should be given intravenously in a dose of 1 0 to 1 25 mg and repeated in doses of 0 25 to 0 5 mg four to six hourly until some effect is observed or until 2 25 mg have been administered when subsequent doses must not exceed 0 25 mg Intravenous digoxin achieves its maximum effect in half to one hour if injections are given two hourly the dose should not exceed 0 25 mg after a total of 1 5 mg has been reached *An overdose of any digitalis preparation given intravenously may be fatal*

*Ventricular paroxysms* may be terminated by injecting intravenously 3 grains (0 2 G) of quinidine 0 2 to 1 G of procaine amide or 10 to 20 ml of a 20 per cent solution of magnesium sulphate (Boyd and Scherf 1943) Both quinidine in doses of 5 to 10 grains (0 3 to 0 6 G) and procaine amide 0 25 to 0 5 G may be given by mouth at two hourly intervals for four or five doses if the matter seems less urgent Armbrust and Levine (1950) found quinidine was successful when given by mouth in 81 per cent of cases—mostly ischæmic Procaine amide has a greater margin of safety than quinidine when given intravenously in the customary dose

*The treatment of resistant cases* of all forms of paroxysmal tachycardia may be very difficult It is essential first to establish the nature of the tachycardia beyond question a common error being to mistake supra ventricular tachycardia with functional bundle branch block for ventricular tachycardia and hence to press home the wrong treatment Next heart failure must be treated vigorously if present, by all the usual remedies for when this is controlled normal rhythm may often be restored and maintained more easily Any underlying cardiovascular disease amenable to treatment such as hypertension thyrotoxicosis mitral stenosis and cor pulmonale should not be neglected Other contributory causes should also be recognised and dealt with if possible these include anxiety insomnia pregnancy alcohol bronchial carcinoma and other intrathoracic diseases If despite attention to such details the attack cannot be terminated or normal rhythm cannot be maintained for long the situation may be very serious Propyl thiouracil, starting with 300 mg daily, is worth trying Bilateral stellate and upper dorsal ganglionectomy abolished paroxysmal atrial tachycardia in several difficult cases reported by White and Bland (1950) but proved valueless in a case of the author s

When standard methods of treatment fail it is usually more profitable to review what has already been done in the hope of finding some fault in management that can be corrected than to resort to generally less effective methods of treatment such as syrup of ipecacuanha half an ounce (15 ml ) as an emetic (Weiss and Sprague 1937) or atebrin 0 1 G intravenously 0 5 G in 10 ml of 1 per cent novocaine intramuscularly or 0 1 G three times daily orally (Gertler and Yohalem 1947)

*Maintenance therapy*

To prevent attacks of all kinds the best treatment is undoubtedly quinidine sulphate gr 3 to 15 (0 2 to 1 0 G ) three times daily Heavy doses may not be tolerated but should be tried boldly if necessary (Gold 1950) Procaine amide 0 25 to 0 5 G three times daily, is also very useful particularly to prevent ventricular tachycardia A maintenance dose of digitalis may be best for atrial tachycardia and oral prostigmin 5 mg t d s if tolerated for nodal tachycardia

When attacks are infrequent short lived easily stopped and not disabling maintenance therapy is not advised for all the drugs mentioned may have undesirable effects on the patient s health and well being Procaine amide for example may cause agranulocytosis

## *PAROXYSMAL TACHYCARDIA ASSOCIATED WITH PRE EXCITATION*

The condition first described as physiological bundle branch block with short P R interval (Wolff Parkinson and White 1930) is due to premature excitation of one or other ventricle usually the right resulting from an anomalous connexion between the A-V node or right atrium and the right

ventricle (Holzman and Scherf 1932) or to accelerated conduction of a portion of the excitatory process at the A V node (Prinzmetal *et al* 1952) probably the latter Electrocardiography shows widening of the QRS complex as in bundle branch block but at the expense of the P R interval which is shortened proportionally the P S interval as measured from the beginning of P to the end of the QRS complex remaining unchanged (fig 6 38) The appearances usually resemble left rather than right bundle branch block The anomalous pathway may be through the bundle of Kent (Wood Wolferth and Geckeler 1943 Kent 1914) or through abnormal conducting fibres arising from the upper part of the bundle of His (Wolferth and Wood 1933) such as those described by Mahaim (1931) The passage of the excitatory impulse down such an alternative pathway might well account for premature right ventricular stimulation Experimental short circuits of the kind envisaged were devised by Butterworth and Poindexter (1942) the classical appearances of the Wolff Parkinson White syndrome resulted On the other hand, Prinzmetal *et al* (1952) found that experimental W P W complexes produced by

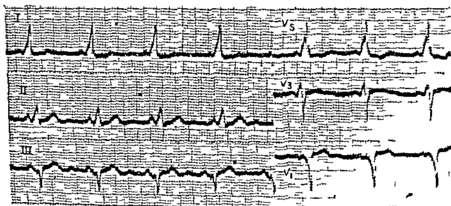



Fig 6 38—Pre excitation

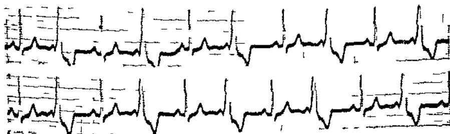


Fig 6 39 ... ng pr ... citation

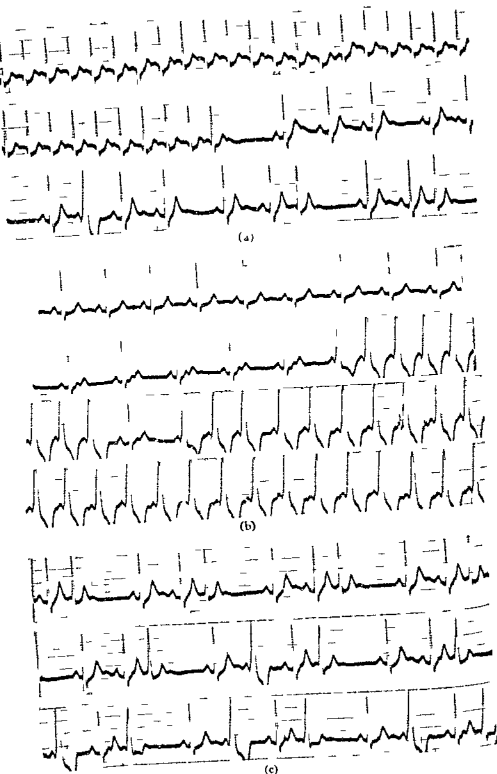



Fig 6 40—Wolff Parkinson White Syndrome showing
(a) Paroxysmal tachycardia with normal QRS complexes (b) Paroxysmal tachycardia with widened QRS complexes (c) Atrial re entry following the major attack

P W ← Post CARDIAC infarction
Irritable focus of the vent



continuous subthreshold electrical stimulation of the A V node would not arise if the bundle of His was cut that W P W complexes sometimes occurred during cardiac catheterisation when the nodal tissue might be injured and after posterior cardiac infarction when the nodal tissue was proved to be injured at subsequent necropsy and that a ventricular form of W P W syndrome existed both clinically and experimentally in which pre excitation was due to an irritable focus in the ventricle Prinzmetal points out that one of the major functions of the A V node is to hold up the excitation wave sufficiently long to allow the atria to contract well ahead of the ventricles and that impairment of nodal function should therefore lead to accelerated conduction (Borduas *et al* 1955) Experimental damage to the A V node may certainly have this effect

The condition is usually congenital occurs in both sexes equally and is often unstable as shown by serial electrocardiograms indeed normal and abnormal complexes may alternate (fig 6 39) On the whole normal conduction is encouraged by atropine abnormal conduction by cholinergic activity (Duthie 1946) The heart is otherwise normal in at least 70 per cent of cases Pre excitation is clinically and academically important on account of its association with paroxysmal tachycardia, and is easily overlooked because casual electrocardiograms may be normal Paroxysmal tachycardia occurs in 50 to 70 per cent of cases (Willius and Carryer, 1946 Wolff 1954) and is often closely related to effort Electrocardiograms obtained during attacks suggest that their mechanism may depend upon a circus movement the impulse travelling down the bundle of His and back through the short circuit (fig 6 40a) or down the short circuit and back through the bundle of His (fig 6 40b) the former being more common Both types of paroxysm may occur in the same patient as in the illustrations In this particular case the second type of paroxysm was provoked by mecholin and before normal rhythm was resumed there was a period of transition in which abnormal P waves appeared immediately after certain QRS complexes (fig 6 40c) causing a single premature ventricular beat and suggesting circus movement due to retrograde conduction through the bundle of Kent or similar structure initial excitation having passed through the bundle of His Similar P waves may be seen in the upper half of figure 6 40b but these fail to excite the ventricles If Prinzmetal s hypothesis is correct paroxysmal tachycardia is presumably nodal and may be regarded as another manifestation of disordered nodal function Occasionally attacks resemble auricular flutter or fibrillation and the ventricular rate may be exceptionally fast A case described by Littmann and Tarnower (1946) had an irregular ventricular rate of 340 per minute Paroxysmal tachycardia may also occur in patients with a short P R interval and without the W P W syndrome Thus Lows *et al* (1952) found it in 9 5 per cent of 200 such cases When all cases with short P R interval and paroxysmal tachycardia were considered only 18 per cent had the Wolff Parkinson White syndrome

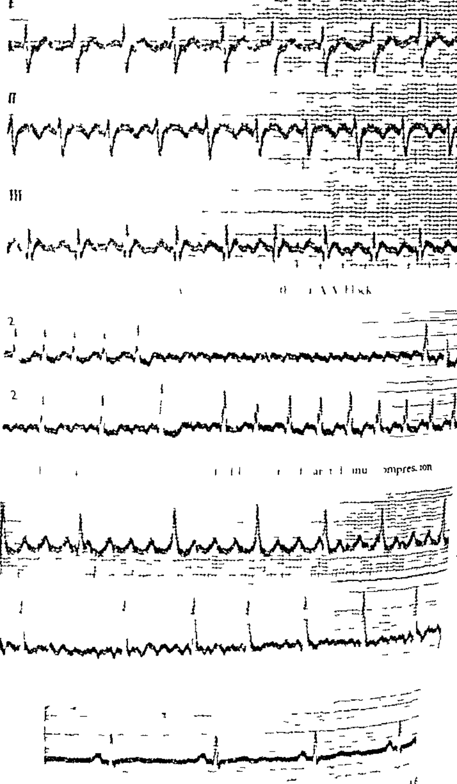



Fig. … Auricular flutter treated with digitalis. Auricular fibrillation … induced … on withholding the drug normal rhythm is resumed

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## AURICULAR FLUTTER

*Physiology* Auricular flutter in man was so named by Jolly and Ritchie (1910) after obtaining the first electrocardiographic records of the condition and was attributed to a circus movement by Lewis (1918–20) The excitatory impulse was believed to travel round a ring of atrial tissue such as the mouths of the venæ cavæ as proved possible by the physiological researches of Mines (1913) Rosenblueth and Ramos (1947) apparently confirm Lewis views Using a high speed cinematograph technique however, Prinzmetal (1950) has disproved this thesis and has shown that auricular flutter and fibrillation like atrial ectopic beats and paroxysmal atrial tachycardia, depend upon the presence and behaviour of an irritable focus in atrial muscle The speed of the auricular beats ranges between 260 and 340 per minute and its rhythm is regular. As the A V node can rarely transmit impulses faster than 210 to 220 per minute, physiological heart block results the ventricles usually responding to every second impulse If the auricular rate is slower however and approaches 200 per minute as it may under the influence of quinidine the ventricles may be able to keep pace (Lewis 1925) If vagal tone is increased as by carotid sinus pressure a greater degree of physiological block results and an A V ratio of 4 1 or so may be established the speed of the *f* waves remaining unaltered Sometimes the ventricular response is irregular

*Clinical features incidence and etiology* Clinically flutter should be suspected in any patient presenting a regular heart rate of 120 to 170 per minute, uninfluenced by effort emotion or change of posture whether there are other indications of heart disease or not When the ventricular response is irregular the first heart sound varies in intensity according to the time relationship between atrial and ventricular contractions (Harvey and Levine 1948)

Flutter is a relatively uncommon but capricious rhythm and may occur when least expected It is twice as common in men as in women and its incidence increases with age being rare under 30 and most frequent (88 per cent) between the ages of 40 and 70 It is very rare in otherwise normal individuals it may complicate such diverse conditions as meningitis pneumonia cholecystitis or carcinoma of the colon In 90 per cent of cases however it is associated with organic heart disease especially rheumatic hypertensive ischæmic or pulmonary, and may then precipitate or complicate congestive heart failure According to Campbell (1947) angina pectoris develops in 25 per cent of paroxysms Attacks are commonly transient, and have the same abrupt onset as paroxysmal tachycardia but they tend to last longer, being measured in weeks rather than hours and may occasionally persist for years Lewis (1937) described a case in a parson which had continued for 24 years

*Diagnosis* is facilitated by carotid sinus pressure, which often causes abrupt temporary slowing of the ventricular rate as described previously whereas in sinus tachycardia slowing is commonly slight and in paroxysmal

tachycardia it is usually absent unless the attack is terminated Electrocardiography is advised in all suspected cases, however and reveals a continuous series of rapid regular atrial 'f' waves (fig 6 41) without intervening iso potential periods When there is 2 1 block, one f wave is more or less obscured by the QRS complex so that the nature of the

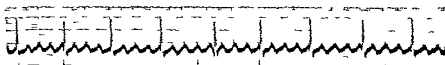


Fig 6 41—Auricular flutter with 4–1 A V block

tachycardia may remain uncertain (fig 6 42) Carotid sinus pressure aids analysis by increasing the degree of block and so unmasking such hidden f' waves (fig 6 43)

*Treatment* The patient should be put to bed and treated with adequate doses of digitalis, beginning with 8 grains (0 5 G) of the powdered leaf followed by 4 grains (0 25 G) and then by 2 grains (0 13 G) at six hourly intervals and continuing with 2 grains (0 13 G) t d s, until serial electrocardiograms show that auricular fibrillation has been established The drug is then withheld in the hope that normal rhythm may be resumed spontaneously (fig 6 44) Electrocardiographic control is necessary because the slow irregular ventricular response that results from such doses of digitalis is no proof of auricular fibrillation under the circumstances Adequate supervision is important owing to the heavy dose of digitalis usually required to induce fibrillation and if toxic symptoms appear dangerous before this result is achieved the attempt may have to be abandoned The effect of digitalis is twofold, as already indicated it encourages the irritable focus to assume the properties associated with auricular fibrillation and by depressing conduction in the bundle of His, it slows the ventricular rate. It was hitherto believed that normal rhythm was resumed when the circus movement was broken by the head of the wave meeting a refractory tail (Lewis 1925) for circus movement could not occur unless there was a gap of responsive tissue just ahead of the wave Digitalis, either during its administration or when it was suspended was thought to close the gap by having an unequal and favourable effect on conduction and on the refractory period Obviously, if conduction were quickened and the refractory period prolonged in atrial tissue the hypothetical gap would close Naturally no drug has this effect those quickening conduction also shortening the refractory period (like the cholinergic bodies) and vice versa (like quinidine) The action of digitalis is complicated by its cholinergic effect the f waves are never retarded, but they may be accelerated especially in those cases that are made to fibrillate (Wedd 1924)

Quinidine should not be given alone to cases of flutter in the first instance for by depressing the irritable focus and slowing the atrial rate, it may

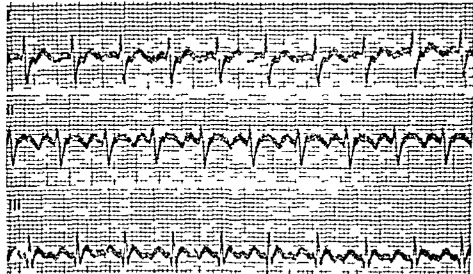


Fig. 6.42—Auricular flutter with [illegible] A-V Block

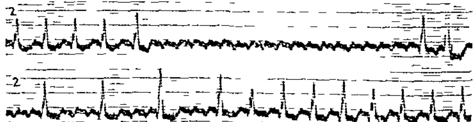


Fig. 6.43—Auricular flutter clarified by use of carotid sinus compression

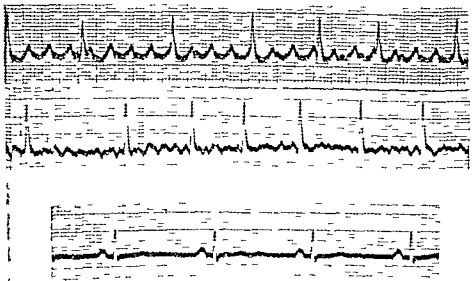


Fig. 6.44—Auricular flutter treated with digitalis. Auricular fibrillation is induced first; on withholding the drug, normal rhythm is resumed.

allow the ventricles to keep pace rapid tachycardia resulting When auricular fibrillation has been established however the resumption of normal rhythm may be encouraged by quinidine in doses of 5 to 10 grains (0 3 to 0 65 G) two hourly to a maximum of 40 to 45 grains (2 5 to 3 G) in one day Quinidine may be given safely to resistant cases of flutter so long as the ventricular response is blocked by digitalis

If flutter continues despite all efforts to break it the patient should be kept on a maintenance dose of digitalis sufficient to control the ventricular rate but the result is rarely satisfactory for short of digitalis intoxication tachycardia due to 2 1 ventricular response is apt to develop on little provocation

In all cases attention should be paid to any associated disease cardiac or otherwise and to combating congestive heart failure

## AURICULAR FIBRILLATION

*Physiology* According to Prinzmetal (1950 1952) two types of atrial contractions may be seen by means of a high speed cinematograph in experimental auricular fibrillation induced by means of aconitine or electrical stimulation (1) minute irregular contractions which he has called *M contractions involving a small area of atrial wall (0 03 × 3 mm)* and (2) large rhythmic wave like contractions (L contractions) which *sweep across the atria 400 to 600 times per minute without pursuing a* circus pathway Blocking a hypothetical circuit round the mouths of the *venæ cavæ had no effect on these waves Direct atrial leads recorded* by means of a cathode ray oscillograph showed very small M waves at 10 000 to 40 000 per minute and *large f waves corresponding to the L* contractions The M waves did not occur in flutter Lewis s theory of circus movement appears to be untenable

At f wave speeds of 320 to 380 electrocardiograms from chest leads placed over the right atrium show f waves which at times are regular and even as in flutter and which at other times are irregular and uneven as in fibrillation (fig 645) At faster rates the f waves are always irregular in time and shape and the ventricular response is commonly rapid and chaotic varying between 100 and 200 per minute (fig 646) Sometimes and of course in treated cases when there is partial atrio ventricular *block the ventricular rate is relatively slow Occasionally there is complete* heart block (usually in cases treated with digitalis over a long period of time) and the ventricular rate is not only slow but regular (fig 647)




Fig 645 —Lead CR1 showing coarse auricular fibrillation or impure flutter

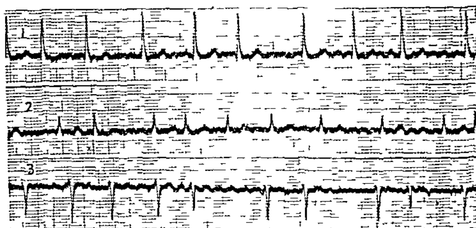



Fig 6 46—Auricular fibrillation

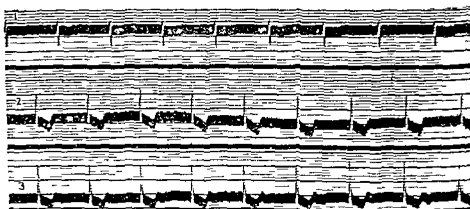



Fig 6 47—Auricular fibrillation with complete A V dissociation due to digitalis

The physiology of the circulation is disturbed by auricular fibrillation in several ways First the lack of atrial help deprives the heart of one of its reserves for powerful atrial contraction can increase the diastolic volume of the ventricles and so augment the force of their contraction second the ventricular rate is often fast enough to prevent proper cardiac filling so that the cardiac output falls—left ventricular filling is especially impaired with fast rates in mitral stenosis third the chaotic rhythm interferes with the mechanical efficiency of the heart many of the beats being wasted fourth the nutrition of the myocardium may suffer owing to reduced coronary flow Physiological studies have shown that when normal rhythm is restored the cardiac output rises immediately *even when the ventricular rate was previously controlled* by means of digitalis (Hansen *et al* 1952)

*Etiology* Auricular fibrillation is characteristically associated with mitral stenosis and toxic nodular goitre and is usually permanent with the former and paroxysmal with the latter It is not uncommon however in the later

stages of hypertensive and ischaemic heart disease On the other hand it is rare in congenital heart disease in bacterial endocarditis (2 per cent) in any form of active carditis in young people in aortic valve disease (unless there is stenosis of the coronary ostia) in pulmonary heart disease in the high output group (apart from thyrotoxicosis) and in pericarditis (although it occurs in 33 per cent of cases of Pick s disease) Like flutter more over *auricular fibrillation may occur in patients with no other evidence of heart disease* it may complicate head injuries meningitis pneumonia and other infections in rare instances, and it may even be found in apparently healthy persons *The most important single factor determining the inci dence of auricular fibrillation in those diseases that favour its occurrence is the advancing age of the patient*

*Clinical features* Symptoms may be absent or negligible or the patient may complain of palpitations If the ventricular rate is very rapid syncope or angina pectoris may result as with flutter and paroxysmal tachycardia The mechanical inefficiency and nutritional hazards resulting from the rapid irregularity of the heart beat often lead to congestive failure when *there is underlying heart disease on the other hand auricular fibrillation* may be precipitated by congestive failure from other causes

*Diagnosis* The clinical diagnosis rests upon the recognition of a chaotic cardiac rhythm *i e one without any semblance of order* and must be dis tinguished from sinus arrhythmia, from ectopic beats, and from auricular flutter with an irregular ventricular response. Sinus arrhythmia should be recognised by its relation to respiration and ectopic beats by the perception of some fundamental order but multiple atrial ectopic beats may be most confusing The cervical venous pulse should be carefully inspected the presence of *a* waves cannon waves or a convincing *v* descent excludes auricular fibrillation Electrocardiography however is advised in all sus pected cases

*Treatment* All cases in which the ventricular rate is accelerated should be treated with digitalis When there is no urgency a simple and safe method is to give powdered digitalis leaf, 3 grains (0 2 G ) t d s on the first day 2 grains (0 13 G ) t d s on the second and 1 grain (65 mg ) t d s there after until the ventricular rate is controlled Subsequently a maintenance dose of 1 grain (65 mg ) twice daily is usually sufficient When a quicker effect is desired the method described for cases of auricular flutter is advised *If digoxin is preferred to digitalis folia* equivalent doses may be used for the slow method of digitalising a patient and 1 5 mg 1 mg and 0 5 mg six hourly for the rapid method In urgent cases with very rapid ventricular rates and severe congestive heart failure digoxin by the intravenous route may be preferable, but is not without danger, and *should never be given in full doses to any patient who may have had digitalis within the previous six weeks* or who still shows a digitalis effect in the electrocardiogram The initial maximum dose is 1 5 mg , but 1 mg is safer and this may be followed by 0 5 mg and then by 0 25 mg at

intervals of not less than two hours and not more [illegible] hours In favourable circumstances the ventricular rate may be [illegible] within half an hour an oral maintenance dose should then [illegible] intravenous doses just recommended Strophanthin may [illegible] of digoxin as Ouabain it may be given in an initial dose [illegible] intravenously, followed by 0 5 mg and then by 0 2 mg [illegible] until the desired effect is obtained As strophanthin [illegible] than forty eight hours it is preferable to digoxin [illegible] effect is not desired

Other preparations of digitalis may be given [illegible] dose being calculated according to the following table of [illegible] strength

| | |
|---|---|
| Powdered digitalis leaf | [illegible] |
| Tincture of digitalis | 1C [illegible] |
| Digoxin | 0 [illegible] |
| Digitoxin (Nativelle's Digitaline) | 0 C[illegible] |

The practitioner is advised to become thoroughly familiar with a few reliable preparations Digoxin and digitoxin have the advantage of being pure crystalloids of fixed potency Digoxin is excreted more quickly than digitoxin The tincture loses strength with the passage of time and when mixed with other drugs and is therefore least reliable The powdered leaf has been the standard preparation in this country for many years but is being gradually displaced by digoxin

Toxic symptoms include anorexia nausea vomiting diarrhœa ectopic beats nodal rhythm heart block, paroxysmal tachycardia and sudden death from ventricular fibrillation Nausea and coupling due to ectopic beats are the best indications that the accumulated dose of digitalis is approaching dangerous concentration Unfortunately the worse the heart the closer the therapeutic dose becomes to the toxic the margin is never great The vagal effects may be relieved by atropine

The correct maintenance dose must be worked out for each individual receiving the drug but it averages 0 5 mg of digoxin daily ranging between 0 25 and 0 75 mg The average maintenance dose of digitoxin is 0 1 mg daily, and is very well tolerated by patients prone to nausea and vomiting because it does not irritate the gastric mucosa

Attempts to restore normal rhythm with quinidine should be made in all cases in which there is no evidence of intrinsic heart disease and especially in cases of successfully treated mitral stenosis or thyrotoxicosis also perhaps when auricular fibrillation is thought to have occurred prematurely or unexpectedly having been precipitated by some passing infection such as tonsillitis or pneumonia or by some other factor which either no longer operates such as pregnancy or which is itself controllable such as dental sepsis When fibrillation develops in the natural course of heart disease however, e g in cases of mitral valve disease which are unsuitable for

surgical treatment attempts to restore normal rhythm end in immediate or remote failure and should therefore be avoided as the procedure is not without risk

Quinidine should be given by mouth in doses of 5 grains (0 3 G) two hourly on the first day followed by 10 grains (0 6 G) two hourly on the second and by 15 grains (1 G) two hourly on the third to a maximum of 40 to 45 grains (3 G) per day the course being terminated immediately the rhythm returns to normal A maintenance dose of 5 grains (0 3 G) t d s is continued for a month in successful cases

Quinidine depresses the activity of the irritable focus, retarding its periodicity and often abolishing it altogether (about 75 per cent of cases) As the f waves slow down (fig 6 48) they may assume the regularity

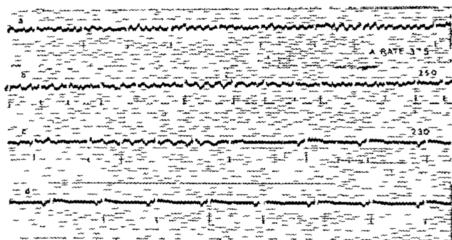



Fig 6 48—Auricular fibrillation treated with quinidine The f waves slow down from 375 to 230 per minute before normal rhythm is restored

of flutter and if their speed approaches 200 per minute there is danger of a 1 1 ventricular response. Tachycardia so provoked by quinidine may be prevented by preliminary digitalis therapy and a maintenance dose of digitalis is advised throughout the quinidine course The theoretical consideration that digitalis and quinidine have partly opposing actions does not prejudice successful practical results

Other complications of quinidine therapy include hypersensitivity and embolism Hypersensitivity may result in generalised œdema urticaria purpura fever vomiting and collapse although such symptoms are rare it is customary to give an initial trial dose of 3 grains (0 2 G) Less important symptoms of quinidine intolerance include epigastric pain nausea diarrhœa tinnitus and diplopia Quinidine lowers the peripheral vascular resistance and when given intravenously may cause syncope

To restore normal rhythm quinidine must usually reach a

concentration of 4 to 10 mgm per litre (Sokolow and Edgar 1950) The maximum blood level is achieved about two hours after an oral dose and then declines gradually over 12 to 24 hours The necessary blood concentration can be obtained when quinidine is given in the manner described above but Sokolow (1951) showed that it could also be reached with doses of 5 to 15 gr (0 3 to 1 G) t d s, the drug being cumulative for a period of three days Yount Rosenblum and McMillan (1952) agree with Sokolow that there are no contraindications to quinidine except hypersensitivity, and that there is no relation between inability to revert to normal rhythm and age, cardiac failure or duration of fibrillation British schools are reserved about accepting this conclusion

Important systemic emboli occur in about 5 per cent of all cases in which normal rhythm is restored and are due to the expulsion of left atrial thrombi There is reason to believe that only fresh thrombi are liable to be dislodged, and that these are most likely to form when the ventricular rate is rapid i e at the onset of the attack before digitalis has been given especially in cases of mitral stenosis when the left atrium and its appendage are dilated Since normal rhythm is more likely to be resumed spontaneously or as a result of medical treatment at this time than at any other and since in fact systemic embolism is known to be a not uncommon complication of auricular fibrillation at this crucial time *whether normal rhythm is resumed or not* there are good grounds for treating all such cases with anti coagulants until the ventricular rate is properly controlled or normal rhythm is resumed and for withholding quinidine until the clotting mechanism has been depressed for at least five days—at any rate in cases of mitral valve disease Intracardiac thrombi are rare in thyrotoxic heart disease even under the most unfavourable circumstances owing to the rapid circulation associated with it

*Lone auricular fibrillation* also increasingly frequent as age advances may be paroxysmal or permanent In about 10 per cent of cases it causes congestive heart failure (Phillips and Levine 1949) and even in favourable cases it causes palpitations and reduces effort tolerance Since normal rhythm can be restored with very little risk in about 85 per cent for an average period of about two years in those that relapse and permanently in 10 or 20 per cent of cases the general tendency to treat conservatively with or without digitalis is open to criticism Heart failure when it occurs is reversible

*Auricular fibrillation flutter and sinus bradycardia* alternating in the same patient usually middle aged or elderly and otherwise normal can be very troublesome Short periods of cardiac standstill may result in syncope or very slow rates may give rise to weakness and dizziness when atrial flutter or fibrillation supervenes some patients actually feel better but complain of palpitations Treatment with atropine in the belief that both the abnormal atrial rhythm and the sinus bradycardia were due to increased vagal tone has proved disappointing

## VENTRICULAR FIBRILLATION

Faradic stimulation of the ventricles invariably induces incoordinated fibrillation of the muscle which usually persists after cessation of the exciting cause The heart muscle is unable to expel its contents and syncope occurs abruptly Spontaneous recovery may occur especially in young healthy animals but sudden death is the rule When the heart is unduly excitable as in asphyxia digital pressure or gently scratching the surface




Fig 6 49—Ventricular fibrillation causing sudden death in a case of ischæmic heart disease

of the ventricle with a pin may be sufficient to induce ventricular fibrillation (MacWilliam 1887) Certain drugs may initiate the phenomenon notably adrenaline chloroform and digitalis Coronary occlusion is also known to be an exciting cause

Clinically ventricular fibrillation is often responsible for sudden death especially in ischæmic heart disease (fig 6 49) aortic stenosis syphilitic aortic incompetence diphtheritic carditis and complete heart block It also explains sudden death following intravenous injections of digitalis mercurial diuretics adrenaline and other drugs It is a rare complication of cardiac catheterisation and it occurs occasionally during or shortly after operations on the heart

Treatment is of little avail The intracardiac injection of quinidine sulphate 3 to 5 grains (0 2 to 0 3 G) or of 500 mg of pronestyl may be tried if circumstances are favourable Quinidine or pronestyl may also be given by mouth as a prophylactic agent when the risk of ventricular fibrillation is great A special electric defibrillator has been developed for surgical use and with cardiac massage may be life saving

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# HEART FAILURE

HEART failure has been defined as a condition in which the heart fails to discharge its contents adequately (Lewis 1933) The words may be applied logically to the heart as a whole or to one or other ventricle The increased residual stroke volume of the failing human heart implied by Lewis definition has been confirmed by modern work (e g Nylin 1943 1945 Friedman 1950) Normally there are said to be about 99 ml of blood left in the right ventricle at the end of systole the ratio $\frac{\text{residual volume}}{\text{stroke volume}}$ being around 1 75 (probably nearer 1 5) in advanced right ventricular failure the residual stroke volume may average as much as 500 ml and the ratio 13 6 (Bing *et al* 1951)

Alternatively Heart failure may be defined as a state in which the heart fails to maintain an adequate circulation for the needs of the body despite a satisfactory venous filling pressure (the condition excludes extracardiac circulatory failure from hæmorrhage vasovagal syncope or shock)

## MECHANISM

The mechanism and even the definition of heart failure have been debated for over a century and are still a source of controversy The back pressure theory so well expressed by James Hope in 1832 which incorporates the idea of independent ventricular failure maintains that when a ventricle fails to discharge its contents adequately blood accumulates behind it and the pressure rises in the respective atrium and venous system After holding sway for nearly a century this conception was replaced by the forward failure hypothesis of Mackenzie (1913) who believed that congestion depended upon failure of sufficient propulsion from behind and who insisted that the heart failed as a whole Before the second world war opinion reverted sharply to Hope s view the arguments in its favour being well marshalled by Harrison (1935) and by Fishberg (1939) but the newer methods of investigation which provided much of the data upon which these arguments were based were crude and subsequent technical refinements have disproved many of them The introduction of cardiac catheterisation to the U S A by Cournand and Ranges (1941) and to Great Britain by McMichael and Sharpey Schafer (1944) provided a new tool for studying the circulation in man and modern hypotheses concerning the mechanism of heart failure have been much influenced by the pioneer work of these investigators (Cournand 1952 McMichael 1947 1948)

The clinical facts are superficially simple enough In predominantly

left sided lesions such as hypertension and aortic valve disease certain compensatory mechanisms are brought into play which help the left ventricle to shoulder its additional burden without embarrassing the organism as a whole Sooner or later and for one reason or another these adjustments no longer suffice and dyspnœa develops at first only on effort and then even at rest while orthopnœa and paroxysmal cardiac dyspnœa colour the clinical picture X rays show pulmonary venous congestion but the jugular venous pressure may be normal and there may be no œdema This syndrome is called *left ventricular failure* In purely right sided lesions such as primary pulmonary hypertension and isolated pulmonary stenosis the breakdown of compensatory adjustments (decompensation) results chiefly in fatigue elevation of the systemic venous pressure distension of the liver and dropsy while the lungs remain dry and radiologically clear This syndrome is called *right ventricular failure* Not infrequently cases of hypertensive heart disease or aortic valve disease start with left ventricular failure and later develop a rise of systemic venous pressure enlargement of the liver and dropsy this is called *congestive heart failure* A number of conditions that affect the heart as a whole such as isolated myocarditis may develop characteristic features of both left and right ventricular failure more or less simultaneously this too is called congestive heart failure In all the conditions so far mentioned there are usually signs of an impaired peripheral circulation as well due to a low cardiac output In the hyperkinetic circulatory states, however such as thyrotoxicosis anæmia arteriovenous fistula beri beri Paget s disease of bone advanced hepatic disease and anoxic cor pulmonale signs of congestive heart failure (both pulmonary and systemic) may be associated with warm hands throbbing digital vessels distended forearm veins and other evidence of an increased peripheral blood flow and raised cardiac output To distinguish these two types of failure McMichael introduced the terms low and high output failure The question at issue is just how all these manifestations of heart failure are brought about and what unifying principles underly them?

## *CARDIAC RESERVES*

The terms compensation and decompensation are intended to define the physiological situation in respect of the cardiac reserves In compensated cases reserve mechanisms come into play which enable the diseased heart to carry on its prime function of maintaining an adequate circulation to all parts of the body without disturbing the function of any organ In mitral stenosis for example a rise of left atrial pressure may compensate for the obstruction but if this rise is too great pulmonary œdema interferes with the function of the lungs and endangers life even though the cardiac output is maintained Decompensation means that the heart can no longer maintain an adequate circulation for the needs of the body all reserves having been used At first this occurs only on effort (limited effort

tolerance) but finally even at rest (heart failure proper) To understand heart failure therefore it is necessary to know just what these reserves are and how they may break down

*The strength of cardiac contraction*

The most obvious way for the heart to meet an extra load would be for the muscle to contract more strongly in the manner of voluntary muscle It has long been known however that heart muscle always responds in precisely the same fashion to any strength of stimulus provided its intrinsic state is unaltered This is the all or none law (Bowditch 1871) It means that all fibres contract fully every heart beat so that at first sight there appears to be no room for a reserve mechanism here The proviso however is important for the intrinsic state of the muscle may well change not only from day to day but even from beat to beat There is good evidence for example that increased sympathetic tone augments the strength of cardiac contraction (Wiggers and Katz 1920) and that increased vagal tone weakens it (Peterson 1950) Stead Hickman and Warren (1947) believe that minor changes of cardiac output from minute to minute may well be a function of varying sympathetic tone Increased adrenergic activity may thus be regarded as the first reserve, and one that can be called upon almost instantaneously Artificial help of the same kind can be given by injecting adrenergic drugs

The strength of cardiac contraction must also be greatly influenced by any factor that alters or interferes with the natural biochemistry of heart muscle (Olson and Schwartz 1951) Digitalis may supply artificial biochemical aid

*Hypertrophy of the heart*

Hypertrophy of the heart muscle is the natural long term method of increasing the strength of cardiac contraction Heart muscle fibres cannot multiply but they can increase in length and bulk This reserve is limited by nutritional difficulties for the nutritional needs of each muscle fibre depend on its cubic volume whereas its nutritional supply is proportional to its surface area thus as the fibre grows in volume there is an increasing disparity between demand and supply the former increasing by the cube the latter by the square Moreover the capillaries upon which the nutrition of the heart muscle depends do not increase as the heart hypertrophies (Katz 1954) Thus there may come a time when the heart is too big to be properly nourished

*Increased filling pressure and cardiac dilatation*

In 1884 Howell and Donaldson showed that the dog s heart increased its stroke output in response to an increased venous input More precisely the strength of cardiac contraction depended on the presystolic volume

and tension of the ventricles it was these which determined the magnitude of the all or none response (Frank 1895) In a series of papers Starling and his associates showed that the increase of stroke output that followed an increased filling pressure depended on the degree to which the ventricular muscle fibres were stretched at the end of diastole rather than upon the diastolic pressure itself also that a critical point was reached sooner or later beyond which further dilatation of the ventricles resulted in a fall of output (Starling 1918) In Starling s curve (fig 7 01) in which the cardiac

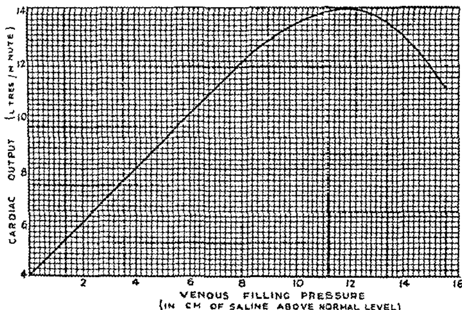



Fig 7 01—Relationship of cardiac output to venous filling pressure (Starling s curve)

output is plotted against the venous filling pressure (right atrial pressure minus the negative intrathoracic pressure) the ascent represents a compensated situation the descent a decompensated or overloaded state It is important to understand that the response of any particular heart to an increased filling pressure varies considerably according to the influence of other factors particularly those affecting the property of myocardial muscle fibres to stretch in response to a rise in diastolic tension (myocardial tone)

The venous pressure may rise primarily as a result of active or passive venoconstriction which reduces the capacity of the venous reservoir or because of an increase in blood volume secondary to sodium and water retention In either event the cardiac output rises and the elevated venous filling pressure is physiological (as on effort) compensatory (as in anæmia) or independent (as in acute nephritis) If the heart is flagging however and fails to empty itself properly its diastolic volume and pressure r

and the elevated venous pressure that results represents a state of decompensation. This overloaded situation may be precipitated by an increase of blood volume resulting from sodium and water retention secondary to impairment of renal blood flow due to reduction of the cardiac output.

A particular form of elevated venous filling pressure results from augmented atrial systole. A good example of this is seen in severe pulmonary hypertension or stenosis when powerful right atrial contraction causing a giant *a* wave in the venous pulse increases the diastolic stretch of the right ventricular muscle and so enhances the force of its contraction (fig 2 22)

*The heart rate*

If the venous filling pressure is maintained the cardiac output rises with increasing heart rates until a critical speed is reached beyond which the output falls rapidly (Henderson 1906). In man the critical rate is around 180, but varies greatly with the state of health of the heart. When the venous filling pressure is maintained tachycardia increases the output because the major part of ventricular filling occurs early in diastole; even at rates of 180 the ventricles may fill almost completely (Rushmer and Thal 1952)

It is not easy to investigate the effect of tachycardia alone on the cardiac output in man because other factors are difficult to keep constant; for instance, tachycardia produced by atropine usually results in a fall of venous filling pressure; adrenalin cannot be used because it augments the force of cardiac contraction; tachycardia produced by exercise is associated with a rise of venous filling pressure and with an increased force of cardiac contraction resulting from release of adrenergic tone.

Certain observations on the effects of paroxysmal tachycardia are pertinent to this subject. When the heart is healthy, rates up to 180 are well tolerated and usually give rise to remarkable polyuria suggesting greatly increased renal filtration. At rates between 200 and 250 polyuria is rare but angina, breathlessness and fatigue are common. At rates over 260 syncope is the rule. Another point of importance is the duration of the tachycardia; bouts lasting a few hours may have features suggesting a raised output such as polyuria, hot extremities and distended forearm veins; if the attack continues for several days, however, these signs may be replaced by those of a reduced output—vasoconstriction, a rise of venous pressure, oliguria, œdema and fatigue, suggesting that the nutrition of the myocardium has become impaired; inversion of the T waves of the electrocardiogram after a prolonged attack confirms this supposition.

In fact it has long been established that the benefits to be derived from tachycardia are limited by four factors: (1) since the duration of systole varies with the square root of the cycle length, diastole shortens disproportionately as the rate increases until proper recovery can no longer take place; (2) at rates above 180 diastole is so short that proper filling is

interfered with (3) as the rate increases the mechanical efficiency of the heart $\left(\frac{\text{work done}}{\text{oxygen consumed}}\right)$ declines (4) the coronary flow which is chiefly diastolic gradually becomes insufficient as the rate increases

Physiologically tachycardia is certainly used as a natural means of increasing the cardiac output and usually accompanies an increased filling pressure and greater adrenergic activity As a cardiac reserve in disease tachycardia is used especially in chronic constrictive pericarditis when it may be almost the sole means of raising the cardiac output and in the hyperkinetic circulatory states such as thyrotoxicosis anæmia and beri beri

## HEART FAILURE

Of these four cardiac reserves the most important in relation to ordinary clinical heart failure is the combination of a raised venous filling pressure and dilatation of the ventricles hypertrophy is a long term matter autonomic influences of relatively fleeting importance and tachycardia rarely fast enough to be disadvantageous (except in paroxysmal tachycardia and uncontrolled atrial fibrillation) Heart failure means that the cardiac reserves no longer suffice to enable the heart to maintain an adequate circulation at rest and that increasing elevation of the venous pressure has distended the labouring ventricle beyond the point of critical diastolic stretch, so that further dilatation results in a fall in output

It is still not entirely clear just what causes the rise of venous pressure McMichael and Sharpey Schafer (1944) suggested that it might be a primary compensating mechanism presumably due to reflex veno constriction somehow excited by an inadequate output but there is no direct evidence in favour of this hypothesis There is no doubt that when a ventricle fails *its diastolic pressure rises this must result in an increased* pressure in the venous system behind the failing chamber There is also no doubt that heart failure results in diminution of renal filtration and total renal blood flow and that retention of sodium and water which is closely correlated with this increases the blood volume and causes œdema (Merrill 1946) the increased blood volume also raises the venous pressure Perhaps all three mechanisms come into play in greater or less degree

### *Forward failure*

In the great majority of cases of heart failure the arterio venous oxygen difference is increased being over 50 ml per litre and the cardiac output reduced being less than 4 5 litres per minute at rest (Stead Warren and Brannon 1948) On effort the cardiac output does not rise but the arterio venous oxygen difference increases greatly (Hickam and Cargill 19 An exception to this general rule is the clinical syndrome of heart f (raised venous pressure hepatic enlargement and dropsy) associate

a raised cardiac output at rest which is found in anæmia beri beri, arterio venous fistula and other hyperkinetic circulatory states In these cases forward failure is relative

The effect of the lowered total output on the various territories of the body has been measured with reasonable accuracy

*The cerebral circulation* as might be expected is usually maintained at or near the normal level of 45 to 50 ml per 100 Gm per minute (Novack *et al* 1953)—about 0 8 litre per minute. Disturbance of cerebral function in heart failure is therefore more likely to be due to hepatic or renal factors than to cerebral hypoxia

*The renal blood flow* normally about 1 3 to 1 5 litres per minute (Smith 1951) is notably reduced to about 0 5 litre per minute while the glomerular filtration rate declines from around 120 ml per minute to 70 or 80 ml per minute (Merrill and Cargill 1948) This is associated with salt and water retention an increased blood volume oliguria œdema and sometimes with a slight rise of blood urea. The low renal blood flow is due to efferent *arteriolar constriction diuresis is always preceded by an increase of renal* blood flow which may be independent of any change in cardiac output and which occurs spontaneously at night (Brod and Fejfar 1950)

*The total hepatic blood flow* averages around 1 500 ml per minute (Bradley *et al* 1945) about 25 per cent of which is carried by the hepatic artery the rest by the portal vein. In heart failure the flow is reduced in proportion to the reduction in cardiac output (Myers and Hickam 1948) and centrilobular necrosis is attributed to anoxia

*The blood flow to the extremities* normally about 1 8 litres per minute (Abramson 1944) is reduced and further peripheral vasoconstriction occurs at once when patients are tilted head down even in left ventricular failure (Brigden and Sharpey Schafer 1950)

*The coronary blood flow* is said to be about 5 per cent of the cardiac output or around 75 ml per 100 Gm of heart muscle per minute i e 225 ml per minute for a 300 Gm heart Using the nitrous oxide method and coronary sinus catheterisation in man Bing *et al* (1949) found the normal left ventricular coronary blood flow averaged 65 ml per 100 Gm of left ventricular muscle per minute. In congestive heart failure (from rheumatic heart disease) the coronary flow was much the same

*Back pressure*

Elevated ventricular diastolic pressure undoubtedly causes the rise in left atrial and pulmonary venous pressures in left ventricular failure. Kopelman and Lee (1951) found that the intrathoracic blood volume was increased from an average normal of 1 8 litres to 2 7 litres. All divisions of the lung volume are reduced except the residual air, the total lung volume averaging about 1 5 litres less than the predicted normal (Richards *et al* 1951) The discrepancy between the two sets of figures may be due to an

increased amount of extravascular fluid in the lung parenchyma and lymphatics

Elevation of the right ventricular diastolic pressure (aided by an increased blood volume) raises the systemic venous pressure and distends the liver It is still uncertain to what secondary effects the raised venous pressure may give rise but it is not directly responsible for œdema

## CAUSES OF HEART FAILURE

The heart may fail because it is overburdened by a raised ventricular pressure or by a raised cardiac output or because the health of the myocardium is impaired by inadequate or faulty nutrition metabolic disorder intoxication or intrinsic disease High outputs are tolerated better than high pressures but myocardial ill health is probably even more important Contributory factors include physical effort anxiety disturbances of rate or rhythm infection and pregnancy but all these are better expressed in more fundamental terms for example infection may increase the cardiac output and impair the health of the myocardium anxiety may raise the blood pressure in hypertensive heart disease and so forth Precipitating causes of this sort are found in 50 per cent of cases of heart failure (Sodeman and Burch 1938)

Viewing the subject in this way it should be clear that a high cardiac output is no more incompatible with heart failure than is hypertension that a heart capable of pumping ten litres of blood per minute is not necessarily better than one capable of maintaining a diastolic blood pressure of 140 mm of Hg Each is a measure of part of the total cardiac work performed neither alone is a sufficient measure of cardiac efficiency although their behaviour under certain experimental conditions may be Moreover the signs and symptoms of heart failure are largely due to alterations of pressure and volume in the pulmonary or systemic venous systems In left ventricular failure *for example the redistribution of volume is the result of a short* lived discrepancy between left and right ventricular outputs Although the balance must be restored quickly the consequences cannot be rectified *until the process is reversed It should again be clear that such disturbances* cannot be detected by casual estimations of the right ventricular output

## LEFT VENTRICULAR FAILURE

When the left ventricle fails to discharge its contents adequately the pressure rises in the left atrium and pulmonary veins and blood accumulates in the pulmonary circulation

### *ETIOLOGY*

Left ventricular failure may result from any disease which imposes an undue burden on the left ventricle or which interferes with its health These diseases include systemic hypertension from any cause aortic valve disease mitral incompetence myocardial infarction and a number of rare

cardiopathies which may affect mainly the left ventricle. In systemic hypertension the left ventricle may fail either because it is unable to meet the stress imposed upon it or because it is enlarged so greatly that it cannot obtain sufficient nourishment. As the nutritional demands of an individual muscle fibre depend upon its cubic volume and the nutritional supply is limited by its surface area there is an increasing disparity between the two as the muscle enlarges which sooner or later becomes critical (Gross and Spark 1937). In acute nephritis and malignant hypertension a rapid rise of blood pressure may cause left ventricular failure before there has been appreciable hypertrophy of muscle on the other hand in long standing cases of essential hypertension with gross enlargement of the left ventricle failure may occur even though the blood pressure has fallen to within normal limits failure then being attributed to nutritional break down In aortic valve disease in addition to these two factors there may be further interference with nutrition as a result of poor coronary filling due to a low mean blood pressure in aortic stenosis and to obstruction of *the mouths of the coronary vessels in syphilitic aortic incompetence* The cause of failure in uncomplicated ischaemic heart disease with myocardial infarction is due entirely to interference with ventricular nutrition resulting from coronary occlusion

## *PHYSIOLOGY*

When the left ventricle fail to discharge its contents adequately its output falls its residual stroke volume increases its diastolic pressure rises and the pulmonary venous pressure rises if the right ventricle is healthy it continues to pump its normal quota and within a few minutes the total blood volume is redistributed more being held in the lungs and less in the greater circulation than before. With increased diastolic stretch the left ventricle may be able to cope with the situation and the balance between ventricular outputs is restored In other words in pure left ventricular failure the cardiac output is at first maintained at the expense of a dilated left ventricle a raised pulmonary venous pressure and an increased quantity of blood in the lungs Symptoms are due to pulmonary venous congestion and in a sense this is still a compensated state although a none too happy one If the left ventricle becomes overloaded any further rise of pulmonary venous pressure results in a fall of left ventricular output and a vicious circle is established Several things may prevent disaster (1) a high pulmonary venous pressure passively raises the pulmonary artery pressure and so loads the right ventricle (2) sometimes active pulmonary vasoconstriction adds greatly to this load (3) the redistribution of the blood volume may lower the right ventricular output which can only pump what it receives (4) bulging of the interventricular septum into the cavity of the right ventricle may reduce the diastolic capacity of that chamber (Bernheim effect) and (5) the pericardium which tends to limit ventricular distension must exert some increased pressure

on the right ventricle if greatly stretched by enlargement of the left If the pulmonary venous pressure rises beyond 35 mm Hg the patient is in danger of losing his life from pulmonary œdema

## *CLINICAL FEATURES*

The symptoms of left ventricular failure are undue breathlessness on effort orthopnœa paroxysmal cardiac dyspnœa and acute pulmonary œdema The findings include bilateral basal pulmonary rales radiological evidence of pulmonary congestion and hydrothorax diminution of all fractions of the lung volume except the residual air an increased quantity of blood in the lungs increased intrapleural respiratory pressure swings a raised left atrial pressure with steep y descent and prolongation of the pulmonary circulation time The diagnosis is supported by gallop rhythm pulsus alternans and Cheyne Stokes breathing and is confirmed by the *demonstration of a suitable cardiovascular disease e g systemic hyper* tension aortic valve disease mitral incompetence or myocardial infarction

*Undue breathlessness on effort* Breathlessness due to left ventricular failure depends upon pulmonary venous congestion which both reduces ventilation and increases the work of breathing (Christie and Meakins 1934) It is not due to anoxia to an increased CO tension or to a fall in pH

*Orthopnœa paroxysmal cardiac dyspnœa and pulmonary œdema* As these three conditions depend on variations of the same fundamental mechanism they are considered together When a patient adopts the upright or sitting position in order to breathe comfortably he may be said to have *orthopnœa* Although an almost constant sign of left ventricular failure it is by no means pathognomonic for it may be found in severe mitral stenosis bronchial asthma and in pericardial effusion The vital capacity is reduced in all these conditions and is greater in the upright than in the horizontal position but its relationship to orthopnœa is not necessarily direct More over its increase in the erect position is greater than can be explained by descent of the diaphragm The discrepancy is due to concomitant changes in the pulmonary circulation the amount of blood in the lungs being greater perhaps by as much as 500 ml in the horizontal than in the erect position (McMichael 1939) The redistribution of blood depends upon the geographical relationship of the atria to their respective venous systems As the right atrium is nearer the head than the feet the pressure within it rises when the body is tilted head down owing to the influence of gravity The right ventricle responds according to Starling s law and pumps more blood into the lungs in the horizontal than in the vertical position (McMichael 1937) The pressure within the left atrium however which is situated more or less in the centre of the lungs is not directly influenced by gravity and the left ventricular output does not therefore immediately keep pace with the right Only when the left atrial pressure rises propor tionately owing to an increased volume of blood in the pulmonary venous system will the balance be restored As patients with left ventricular failure

already have pulmonary congestion the extra engorgement which results from adopting the horizontal position may prove critical moreover if the left ventricle is already overloaded it will not respond to the rise in the left atrial pressure but will fail the more

*Paroxysmal cardiac dyspnœa* usually occurs at night The patient awakes with a feeling of suffocation and sits bolt upright gasping for breath he may climb out of bed and open a window or walk about in an agitated way

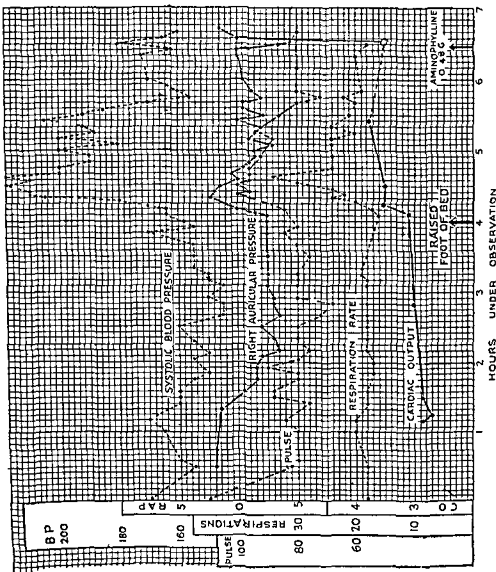



Fig 70 —Graph illustrating typical changes in blood pressure right auricular pressure pulse rate respiration rate and cardiac output in an attack of paroxysmal cardiac dyspnœa initiated in a patient with left ventricular failure by raising the foot of the bed The effect of aminophylline is shown at the end

In cases of simple orthopnœa this behaviour brings immediate relief but in paroxysmal cardiac dyspnœa the feeling of suffocation increases and the struggle for breath lasts for ten to twenty minutes Coughing and wheezing are commonly associated (*cardiac asthma*) and the patient may complain of palpitations faintness or substernal tightness The skin is pale cyanosed and cold indicating profound vasoconstriction and sweating may be profuse The blood pressure and venous pressure are both raised Attacks usually subside spontaneously but may be repeated nightly or at intervals of days or weeks In more severe cases *pulmonary œdema* develops Widespread crepitations are then heard over the lungs and quantities of frothy pink or white watery fluid are expectorated

Such attacks may sometimes be provoked by effort or by a rigor They are easily induced experimentally in susceptible subjects by raising either the venous pressure or the blood pressure by artificial means (fig 7 02) The mechanism probably depends upon acute discrepancy between right and left ventricular outputs, so that both the pressure and volume of blood in the pulmonary circulation reach critical levels Measurements of pressure changes by means of an indwelling cardiac catheter in spontaneous nocturnal attacks indicate that the venous pressure may rise before the blood pressure When attacks are induced by raising the venous pressure the cardiac output may rise Thus although the heart is said to be failing it may in fact be performing more work than usual both with respect to blood pressure and output The laboured breathing may be due in part to the extra effort required to inflate and deflate a turgid lung the intrapleural pressure showing greatly increased fluctuations (Heyer *et al* 1948) In frank pulmonary œdema however ventilation is seriously impaired and dyspnœa is partly due to anoxia

Certain difficulties in our understanding of these attacks must be faced It is by no means clear just why they occur at night or during sleep it has been suggested that depression of the nervous system during sleep allows too great a degree of pulmonary venous congestion to take place before hyperventilation wakes the patient and forces him to lower the right ventricular output by adopting a more upright posture so that relief comes too late to prevent a major attack also that reabsorption into the blood stream of tissue fluid formed during the daytime owing to disturbed renal physiology results in a rise of blood volume and venous pressure which augment right ventricular output and so increase pulmonary venous congestion (Perera and Berliner 1943) But the physical inactivity and muscular relaxation during sleep lower the systemic venous pressure by providing a larger effective venous reservoir and this should help to relieve pulmonary venous congestion again reabsorption of tissue fluid is due to the spontaneous diuresis that takes place during the night in cases of heart failure an event which should also relieve pulmonary venous congestion According to Brod and Fejfar (1950) the increased renal blood flow responsible for nocturnal diuresis is independent of any change in

cardiac output or right atrial pressure Another difficulty is the variable relationship between left atrial pressure and transudation of fluid from the pulmonary capillaries into the alveoli theoretically this should occur whenever the left atrial pressure exceeds the osmotic pressure of the plasma (about 30 mm Hg) but in practice much higher hydrostatic pressures may be recorded in the pulmonary capillaries without pulmonary œdema developing The state of the connective tissue between the alveolar membrane and the capillary may partly explain this for if collagen is much increased here it may serve as a barrier which tends to prevent fluid passing from the capillaries into the alveolar spaces (Hayward 1955) The efficiency of the pulmonary lymphatics in removing protein containing fluid from the walls of the alveoli must also be important Capillary permeability is increased by infection and by anoxia (Maurer 1940) both of which may encourage pulmonary œdema The high protein content of pulmonary œdema fluid (2 to 4 per cent) certainly proves that the capillaries are allowing much protein to escape during the attack (Drinker 1945), and this must greatly reduce the differential osmotic pressure across the capillary membrane Then the part played by bronchospasm must not be overlooked This is a variable complicating factor which increases ventilatory difficulty and the labour of breathing encourages hypoxia and favours the small hours it occurs in about half the cases and is presumably a reaction to congested bronchial mucosa Finally it is by no means clear why the attacks usually terminate spontaneously The great respiratory struggle the mental anguish that goes with it the increasing anoxia and bronchospasm all tend directly or indirectly to encourage the transudate only the natural adoption of the upright position works in the right direction Since acute hypoxia causes pulmonary vasoconstriction (Liljestrand 1948) active pulmonary hypertension might be expected to terminate the attack by reducing the output of the right ventricle but there is no evidence so far that acute pulmonary œdema increases the pulmonary vascular resistance

*Bilateral basal pulmonary rales and hydrothorax* Basal rales diminished air entry into the lower lobes and some impairment of the percussion note at the bases are said to be usual in left ventricular failure but in the author s experience such auscultatory signs are more likely to be absent or misleading Crepitations when due to pulmonary œdema are widespread rather than basal, and when there is no pulmonary œdema râles can only be bronchial *A raised pulmonary venous pressure per se gives rise to no auscultatory signs whatever* If the bronchial mucosa is congested bronchial secretions may be excessive or there may be broncho spasm but these bronchial rales and rhonci are inconstant and unreliable signs of left ventricular failure and are much more commonly due to chronic bronchitis Thus the oft repeated comment concerning the discrepancy between the site of pulmonary venous congestion as viewed radiologically when it is perihilar, and as heard clinically when it is basal is explained by the

simple fact that what is heard is not pulmonary venous congestion Bedford and Lovibond (1941) found that hydrothorax was a common complication of pulmonary congestion from left ventricular failure and that although often bilateral, tended to be more marked on the left side Its occurrence may depend upon the fact that the visceral pleura is drained by the pulmonary rather than by the bronchial veins (Miller 1937) but its precise mechanism is not yet fully understood

*Radiological signs of pulmonary congestion* The increased opacity seen in skiagrams is hilar and probably due to chronic interstitial œdema (fig 7 03) During attacks of acute pulmonary œdema a fleecy mottling spreads out from the hilum on both sides (figs 7 04 and 7 05) Hydrothorax may also be revealed by X rays perhaps when unsuspected clinically Interlobar effusion may be responsible for a rounded transient sometimes migratory opacity—the so called vanishing tumour of the lung Confirmatory evidence of left ventricular failure may be obtained by noting the size and shape of the heart shadow

*Reduction of the vital capacity and lung volume* The vital capacity is reduced by an amount equivalent to the extra quantity of blood and interstitial fluid in the lungs it is reduced much more if there is pulmonary œdema or a large hydrothorax as well and by a further few hundred ml according to the degree of cardiac enlargement Readings of 1 000 to 1 500 ml are common and may be as low as 500 ml when there is pulmonary œdema or hydrothorax



Fig 7 03—Pulmonary congestion in left ventricular failure (case of syphilitic aortic incompetence)

The lung volume is reduced proportionately the residual air remaining unchanged This at once distinguishes the condition from emphysema in which a low vital capacity is associated with a normal lung volume and increased residual air

As stated previously intrapleural respiratory pressure swings are excessive owing to increased resistance on the part of the turgid lung to both inflation and deflation

*Prolongation of the pulmonary circulation time* The normal arm to tongue

circulation time as measured by decholin or saccharin (q v ) averages 13 5 seconds, ranging between 9 and 18 seconds Since the time taken by the substance to travel from the left ventricle to the tongue may be neglected and the journey from the antecubital vein to the right atrium takes only two or three seconds (Blumgart and Weiss 1927) the total arm-to tongue time is governed chiefly by passage through the lungs Using



Fig 7 04—Acute pulmonary œdema from left ventricular failure



Fig 7 05—Acute pulmonary œdema in mitral stenosis

(*A knot l dgm t t D G ham H yward*)

radium C intravenously, which can be detected at any given point in the circulation by means of a special radio sensitive instrument, Blumgart and Weiss also showed that when the systemic venous pressure is raised in con gestive heart failure the delay between the antecubital vein and the right atrium does not exceed five seconds even in gross cases It follows that with pure right ventricular failure the arm to tongue circulation time should not exceed 23 seconds and should often be within normal limits in fact this is so On the other hand in left ventricular failure the average time is 30 seconds (Wood 1936) and may be much longer The delay is due to pulmonary congestion and occurs presumably on the venous side

*The arm to lung time* The arm to lung time as measured by ether or amyl acetate (q v ) is said to be helpful in distinguishing primary left from pure right ventricular failure if the total arm to tongue time is also known When the delay is proximal to the heart as in pure right ventricular failure the arm to lung time is delayed as much as the arm to tongue time on the other hand if there is further delay in the pulmonary veins as in primary left ventricular failure the arm to tongue time is disproportion ately prolonged Although theoretically this test might seem helpful in fact

it is rarely so for two reasons first because the end point in the lung both with ether and amyl acetate is often unreliable and indefinite and second because it is easier and no less accurate to allow 1 to 5 seconds for delay proximal to the heart according to the degree of systemic venous engorgement

*Raised left atrial pressure with steep y descent*

Cardiac catheterisation in cases of left ventricular failure has revealed mean indirect left atrial pressures in the expected range between 10 and 30 mm Hg above the sternal angle Unlike the tracings in mitral stenosis however the pressure drops rapidly after the opening of the mitral valve the down stroke of v or the y descent being remarkably steep the trough y may be followed by a fairly sharp rise of pressure back to the v point (fig 7 06) left ventricular and left atrial diastolic pressures are essentially

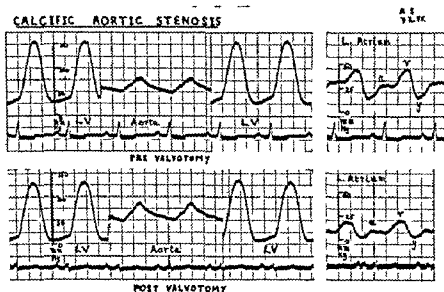



Fig 7 06—Pressure pulses from aorta left ventricle and left atrium in a case of aortic stenosis with left ventricular failure before and after aortic valvotomy showing a typical steep y descent in the left atrial tracing

the same potential differences being offset by unobstructed flow The appearances are similar to those seen in mitral incompetence (Owen and Wood 1955) In the tracing illustrated which was obtained from a case of aortic stenosis with left ventricular failure and recorded during aortic valvotomy the Ry v ratio (q v ) was 5 4 before and 6 after the operation

## GALLOP RHYTHM

When the rhythm of the heart sounds has three instead of two beats per cycle one may properly speak of triple rhythm The term covers all

varieties of cadence in which three heart sounds are heard Gallop rhythm, on the other hand should have a stricter meaning and should be applied only to specified forms of triple rhythm as explained subsequently

*Mechanism* Phonocardiography proves that there are really four normal heart sounds the atrial or presystolic sound associated with atrial systole and late ventricular distension the first heart sound due to mitral and tricuspid valve closure the second heart sound due to closure of the aortic and pulmonary valves and the third heart sound which is attributed to sudden distension of the ventricles in the phase of rapid filling Each of these sounds is thus composed of at least two elements Although these elements may not be strictly synchronous they are sufficiently so as a rule to produce but one obvious sound to the untrained human ear On more careful analysis however they may often be separated sufficiently to be detected individually by auscultation and we may then speak of split sounds The word split describes the sound well and also indicates the mechanism of its production The term reduplication is often used instead, but has less to recommend it for it bears an accidental onomatopœtic resemblance to the sound of presystolic gallop and it is illogical to apply a word that means doubling to an act of division Split sounds do not give the cadence of triple rhythm because of the close proximity of the separated elements

The extra sound that is responsible for triple rhythm is usually an exaggerated atrial sound the third heart sound or a summation of the two Occasionally it is an additional systolic sound of unknown origin

*Presystolic (atrial) gallop* An audible atrial sound associated with a normal or slightly prolonged P R interval gives rise to triple rhythm with an amphibrachic metre (u — u) As it may be felt as well as heard it is best appreciated by means of a rigid wooden stethoscope or with the naked ear so that tactile and aural senses may be allied The presystolic sound is soft and dull, and is usually localised to the region of the apex beat where it is pathognomonic of left ventricular stress occasionally it is heard best at the left border of the sternum when it may denote right ventricular stress The extra sound occurs about 0 15 second after the onset of the P wave and about 0 07 second after the onset of atrial systole (Weitzman 1955) it is attributed to extra forceful ventricular distension If the P R interval is sufficiently prolonged, the atrial sound may fall in mid or early diastole if the heart rate is fast its true relation to the first or second heart sound cannot be determined clinically unless transient slowing is induced by means of carotid sinus compression Presystolic gallop is never heard when there is atrial fibrillation

Presystolic gallop is a sign of ventricular stress That the atrial reserve is being used means that the handicapped ventricle has asked for (and is receiving) extra presystolic stretch to enable it to meet its commitments The sign does not therefore denote failure but a particular form of compensated state

Left atrial gallop is heard chiefly in essential hypertension and following cardiac infarction, right atrial gallop in severe pulmonary hypertension or stenosis.

*Normal third heart sound* When the extra sound occurs shortly after the second heart sound giving the metre of a dactyl (— u u) it may represent a normal or abnormal third heart sound (fig 7 07) The normal third heart

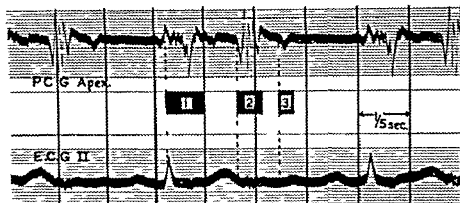



Fig 7 0 —Phonocardiogram showing a normal third heart sound
(R art ; f D F D H (a )

sound was well described by Gibson (1907) It is soft low pitched, and usually accompanied by a palpable shock, it is more or less localised to the apex beat, varies in intensity with respiration and is accentuated when the subject lies on the left side especially if the venous pressure is raised by pressing on the abdomen It may be heard in the great majority of children (but not in infants) in about 50 per cent of young adults occasionally in the middle aged and rarely in the elderly Phonocardiography shows that the third heart sound synchronises with the latter half of the descending limb of the v wave of the jugular phlebogram and therefore with the period of rapid ventricular filling (Ohm 1913) It is attributed to sudden distension of the left ventricle at this time—about 0 15 second after aortic valve closure

*Protodiastolic gallop* Abnormal third heart sounds are common in mitral incompetence, constrictive pericarditis and in advanced heart failure from any cause especially when there is atrial fibrillation The age and clinical condition of the patient emphasise their significance The term protodiastolic applied to this form of gallop is unfortunate for physiologically protodiastole is the first part of ventricular relaxation immediately before and incorporating the second heart sound the second phase in diastole is isometric relaxation with all valves closed the third is the rapid f phase with atrial pressures chasing ventricular pressures to the 3 and it is towards the end of this third diastolic period that the extra

occurs *diastolic gallop* would describe it more simply and without this inaccuracy and would still be sufficiently descriptive to distinguish it from other forms of gallop

Left ventricular diastolic gallop implies a raised left atrial pressure and rapid left ventricular filling, and therefore denies mitral stenosis it also implies absence of those conditions which accentuate the third heart sound without failure e g organic mitral incompetence and Pick s disease, thus by common use the term has come to mean triple rhythm due to an abnormal third heart sound resulting from left ventricular failure or near failure Whether or not it can be due to some alteration of myocardial tone independent of overloading is still uncertain

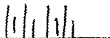
Right ventricular diastolic gallop has a similar meaning in relation to right ventricular physiology and at once denies tricuspid stenosis

*Summation gallop* Summation of atrial and third heart sounds can only occur when there is tachycardia or when the P R interval is sufficiently prolonged With tachycardia the metre may seem to be anapaestic (u u —) dactylic (— u u) or amphibrachic (u — u) according to the fancy of the listener for the extra sound occurs in mid diastole Summation sounds have no clinical significance if they disappear when the heart is slowed by carotid sinus compression (summation gallop) on the other hand such slowing may reveal an atrial sound or a normal or abnormal third heart sound

*Extra systolic sounds* It is not uncommon for an extra sound to occur during ventricular systole Excluding vascular ejection clicks (q v ) there are three varieties—the systolic click of left sided pneumothorax lesser systolic clicks possibly associated with pleuro pericardial adhesions and a third type in which the extra sound is dull and muffled and in no way like a click Patients with partial left sided pneumothorax may complain of a loud clicking or bubbling noise synchronous with the heart beat It may be so loud that it can be heard at a distance of several feet from the patient it varies markedly with respiration and with change of posture and is always transient It is occasioned by the activities of bubbles of air between the heart and surrounding structures and only occurs when the pneumothorax is small, so that clinically it is a late development, appearing when most of the air has been absorbed (Scadding and Wood 1939) Lesser systolic clicks are heard from time to time in subjects who are perfectly well and according to Gallavardin (1913) may depend upon pleuro pericardial adhesions In these cases the extra sound resembles a click but is not so impressive nor so variable as that associated with left sided pneumothorax It may last for weeks months or years and may come and go without apparent reason The third type (systolic gallop) is distinguished from greater and lesser systolic click by the character of the extra sound which is dull and muffled Its mechanism is not yet understood It is uncommon and when heard may be disregarded for it occurs in apparently healthy persons

*Note on nomenclature* Introduced by Professor Bouillaud analysed and popularized by Potain (1876) the term gallop rhythm originally referred to that variety of triple rhythm which denoted impending or actual left ventricular failure and in the presence of tachycardia is marvellously adapted to the sound it designates But by 1900 Potain had extended the meaning of the bruit de galop to include presystolic protodiastolic and systolic varieties attributing these different metres to the same factors that are to day held responsible Thus historically it is not incorrect to regard gallop rhythm and triple rhythm as synonyms but there is an advantage in excluding certain types of triple rhythm from the cadences embraced by the bruit de galop Thus it is preferable and customary to speak of pre systolic (atrial) diastolic systolic and summation gallops on the one hand and of systolic clicks the third heart sound and the opening snap of mitral stenosis on the other

## PULSUS ALTERNANS



Pulsus alternans (Traube 1872) is characterised by a regular rhythm in which the pulse beats are stronger and weaker alternately It may be detected by palpation or more easily by sphygmomanometry there being a difference of 5 to 20 mm of mercury in the systolic pressure between alternate beats It may be found in association with left ventricular failure toxic carditis, paroxysmal tachycardia or auricular flutter Clinically alternation may be maintained as long as the heart is labouring occasionally for as long as two or three years Latent alternation may become manifest when the heart beats faster Experimentally under favourable conditions e g when the heart is poisoned by certain drugs including digitalis when it is made to beat very fast or when its blood supply is curtailed short periods of alternation may follow a premature ectopic beat (Mackenzie 1907–8) or a dropped beat (Hering 1908) Sphygmograms show that pulsus alternans may begin abruptly either with an unusually large beat or with a small beat (Lewis 1925) and that the sum of a large and small beat equals the sum of two normal beats (Gaskell 1882) Pulsus alternans is exaggerated by any agent or manœuvre that lowers the venous filling pressure, and diminished by any procedure that raises the venous filling pressure (Friedman *et al* 1953)

No thoroughly satisfactory hypothesis has been evolved to explain pulsus alternans It is generally believed that fewer muscle fibres contract with the weaker beats than with the stronger owing to the development of a state of partial refractoriness (Lewis 1925) fibres which do not contract with one beat recover in time for the next other fibres which contract with the first beat are still refractory and therefore unready for the second In other words there is a state of 2 1 partial ventricular response But if this were true all the beats should be weaker than normal the hypothesis does not explain the stronger beats Another suggestion is that pulsus alternans depends upon a disorder of ventricular relaxation for the ventricles hold

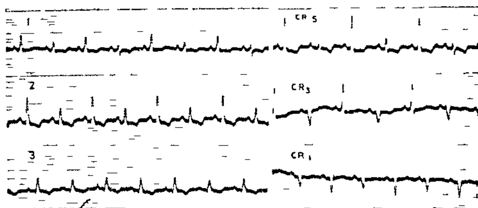



Fig 708—Electrical alternation in a case of malignant disease involving the pericardium pulsus alternans was present

more blood with the stronger beats and less with the weaker (Straub 1917)

Pulsus alternans should not be confused with electrical alternation (fig 708) nor with coupled beats due to premature systoles Electrical alternation is sometimes associated with pulsus alternans however as in the case illustrated

## CHEYNE STOKES BREATHING

Periodic breathing was described by Cheyne (1818) in what was probably a case of hypertensive heart failure with right hemiplegia For several days his breathing was irregular it would entirely cease for a quarter of a minute then it would become perceptible though very low then by degrees it became heaving and quick and then it would gradually cease again this revolution in the state of his breathing occupied about a minute Stokes (1854) connected the phenomenon with serious heart disease

*Mechanism* In spontaneous Cheyne Stokes breathing, the respiratory centre is depressed and appears to be insensitive to a normal carbon dioxide tension but still responds to a raised $pCO_2$ and reflexly to sufficient anoxia With normal arterial oxygen and $CO_2$ tensions breathing therefore stops, during the apnœic phase the arterial $pO_2$ falls and the arterial $pCO_2$ rises and sooner or later this powerful combination excites the sluggish respiratory centre during the dyspnœic phase however the abnormal blood gas tensions are soon corrected and breathing again stops The crescendo character of the dyspnœic phase may be due to time lag when respiration starts and carbon dioxide in the blood entering the lungs is blown off blood which has already passed the pulmonary capillaries must have a higher carbon dioxide tension and lower oxygen tension than that which galvanised the respiratory centre into action this takes 5 to 10 seconds to reach the respiratory centre in normal subjects and an average of about 20 to 25 seconds in patients with left ventricular failure

The administration of carbon dioxide abolishes Cheyne-Stokes breathing by maintaining an arterial $pCO_2$ high enough to excite the respiratory centre The inhalation of oxygen prolongs the period of apnœa because it then takes longer for an effective anoxic stimulus to develop Voluntary hyperventilation precipitates periodic breathing by ensuring an initial period during which the blood gas tensions are such that the respiratory centre must lie idle Natural sleep, barbiturates and morphine aggravate Cheyne Stokes breathing by further depressing the respiratory centre

*Clinical features* Periodic breathing may result from a cerebral lesion e g a head injury or a cerebral vascular accident or from left ventricular failure usually in patients with hypertensive or ischæmic heart disease when sclerosis of cerebral vessels may be associated

The cerebral type is characterised by a rise of blood pressure and pulse rate during the dyspnœic phase (Eyster 1906) in patients with left ventricular failure the central venous pressure and blood pressure rise during dyspnœa the pulse rate and fore arm blood flow during apnœa (Sharpey Schafer 1948) Rhythmic variation in the size of the pupils may also be observed they dilate during dyspnœa and contract during apnœa

Cheyne Stokes breathing may cause insomnia by waking the patient at the height of the dyspnœic phase

## RIGHT VENTRICULAR FAILURE CONGESTIVE HEART FAILURE

When the right ventricle fails to discharge its contents adequately the pressure in the right atrium and venæ cavæ rises the liver becomes enlarged and tender and dependent œdema usually develops

### *ETIOLOGY*

Right ventricular failure in its purest form results from pulmonary hypertension massive pulmonary embolism pulmonary stenosis or atrial septal defect

The term congestive heart failure is preferable when systemic congestion complicates mitral stenosis left ventricular failure rheumatic or other forms of carditis thyrotoxicosis or other hyperkinetic circulatory states serious abnormalities of rhythm ventricular septal defect or other diseases affecting the heart as a whole

### *CLINICAL FEATURES*

*Elevation of the venous pressure* By far the most important sign of right ventricular failure is a rise of systemic venous blood pressure Its detection depends essentially upon clinical observation especially upon inspection of the internal jugular pulse (q v )

In untreated heart failure the venous pressure averages about 10 cm above the sternal angle at 45 degrees, but the range is considerable (3 to 25 cm ) The chief venous pulse wave may be *a* or *v* or the return of

y to the z point When there is auricular fibrillation and no x descent it is difficult to distinguish the venous pulse of heart failure from tricuspid incompetence, but on the whole v is bigger in tricuspid incompetence and is transmitted more obviously to the liver Clinically the distinction rarely matters much for tricuspid incompetence is nearly always functional and secondary to right ventricular dilatation and failure

When the venous pressure is within normal limits at rest, it may yet rise unduly on slight exertion and may take several minutes to regain its resting level This is a manifestation of limited cardiac reserve The jugular venous pressure normally falls on exertion because increased ventilation lowers the mean intrathoracic pressure the true filling pressure tends to rise

The cause of the elevated venous pressure in congestive heart failure has already been discussed (page 267)

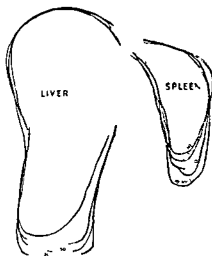



Fig 7 09—Tracings of serial skiagrams of liver and spleen opacified by means of thorotrast demonstrating the rapid shrinkage of the liver and spleen which occurs when 1 5 mg of digoxin is administered to a case of congestive failure

*Enlargement and tenderness of the liver* Hepatic distension may cause spontaneous pain in the right hypochondrium especially when it develops quickly as in failure from paroxysmal tachycardia Sometimes the pain is related to effort

Palpation of the liver should be preceded by inspection and percussion Epigastric fullness and dullness to percussion are characteristic of hepatic engorgement on the other hand epigastric flattening or concavity with resonance to percussion is incompatible with it Percussion of the right hypochondrium during the different phases of respiration often reveals the size of the liver with as much precision as palpation The latter is best carried out with the left hand the physician standing to the patient s left It may be helpful to place the right hand high up under the right lower ribs and to exert forward pressure in order to push the liver towards the anterior abdominal wall if the organ is distended its edge can be felt with the forefinger of the left hand as it moves downwards during inspiration Pressure over an engorged liver is painful Hepatic pulsation may be felt in cases of tricuspid incompetence expansion coinciding with ventricular systole If there is ascites an enlarged liver may be recognised by dipping , a repeated sudden pressure of the hand over the region of the liver when a sensation like that of a patella tap or like that of ballotting a fœtus in utero may be appreciated The liver

shrinks as engorgement is relieved (fig 7 09) and this may be demonstrated within half an hour of giving 1 5 mg of digoxin intravenously (Wood 1940)

Anatomically the liver almost invariably shows centrilobular hepatic necrosis in cases of congestive heart failure—Hepatic function is disturbed to the extent of a raised serum bilirubin (usually short of frank jaundice) increased urobilinogen in the urine and diminished excretion of brom sulphalein alkaline phosphatase total and differential serum proteins and the serum colloidal gold precipitation test are all usually normal (Sherlock 1951)

After repeated attacks of failure or after years of persistent distension cirrhotic changes may occur but they are usually unimportant and rarely interfere seriously with hepatic function or with portal drainage The most important clinical sign of seriously impaired hepatic function appears to be the bright palmar flush often associated with warm hands and digital throbbing despite obviously advanced heart failure and evidence of a low cardiac output



Fig 7 10—Dependent œdema in congestive heart failure

*Œdema* Of the three classic signs of congestive heart failure œdema is the least reliable It may be absent when the venous pressure is high and gross when it is not so high It is frequently absent in acute cases especially in children Cardiac œdema is essentially dependent (fig 7 10) but is occasionally observed in the face and is not infrequent in the arms It is of course accompanied or preceded by oliguria and by a gain in body weight in fact as much as six litres of fluid may collect in the tissue spaces before pitting œdema is necessarily demonstrable

The mechanism of the two most important forms of œdema cardiac and nephritic is not yet fully understood In both as a rule the protein content of fluid samples is low (less than 1 G per cent) the venous pressure is raised, and the blood volume is increased (Warren and Stead 1944) but there are exceptions Thus in chronic anæmia with congestive heart failure the blood volume is much diminished (Sharpey Schafer 1944) Increased capillary permeability is excluded by the low protein content of the œdema fluid moreover the theory that anoxia might be the cause of such capillary

dysfunction is unlikely in that cardiac œdema may be associated with a high cardiac output and normal arterial oxygen saturation as in arterio venous aneurysm Elevation of the hydrostatic pressure at the venous end of the capillaries must play a part but not necessarily a major part In partial superior vena cava obstruction for example œdema does not occur until the venous pressure is very much higher than it is in heart failure and ligation of the inferior vena cava below the renal veins in cases of heart failure relieves œdema in the legs (Cossio and Perratta 1949) Reduction of renal blood flow to about 25 per cent of normal in most cases of congestive failure has been demonstrated (Merrill 1946) and there is a considerable degree of sodium retention according to Merrill and Cargill (1948) œdema occurs when the filtration rate falls below 70 to 80 ml /litre tubular reabsorption being almost complete Merrill and Cargill (1947) demonstrated similar impairment of renal blood flow and filtration rate in a case of thyrotoxic heart failure with high cardiac output

There is also evidence that patients with congestive heart failure excrete an anti diuretic substance in the urine and that this is not pitressin (Bercu Rokaw and Massie 1950) This opens up yet another line of approach to this fascinating problem

## OTHER MANIFESTATIONS OF CONGESTIVE HEART FAILURE

*General symptoms* Owing to the absence of pulmonary venous congestion breathlessness is far less pronounced than in left heart failure and there is no orthopnœa The low cardiac output is reflected by fatigue or by a sense of heaviness in the limbs and on effort there may be dizziness or blurring of vision In severe cases vomiting may be troublesome and it is sometimes difficult to know whether heart failure or digitalis therapy is responsible

*Urinary findings* Oliguria, of course is associated with œdema The urine which is rich in colour and of high specific gravity often contains albumin, leucocytes, red cells, and both hyaline and granular casts

*Hydrothorax* may occur from left or right ventricular failure and though usually bilateral tends to be left sided with the former and right sided with the latter (Bedford and Lovibond 1941) It should be remembered that the visceral pleura is drained by a venous plexus which is composed of both bronchial and pulmonary venous radicles In typical instances the fluid is a transudate with a specific gravity ranging between 1 015 and 1 020 protein is often between two and three per cent and there may be moderate numbers of leucocytes and red cells Unsuspected pulmonary infarction may further complicate the picture increasing the specific gravity the protein content the leucocyte count and especially the number of red cells the overlying pleurisy giving rise to an exudate If the fluid is frankly hæmorrhagic associated pulmonary infarction may be diagnosed with confidence

*Ascites* is less common than hydrothorax and usually implies long standing failure. It is a special feature of tricuspid lesions and of chronic constrictive pericarditis

*Hydropericardium* is usually of little significance cardiac compression does not occur the electrocardiogram is uninfluenced and there are no symptoms It is only important in that it alters the size and shape of the heart shadow and so may confuse radiographic observations

*Cerebral symptoms* Difficulty in concentration impairment of memory mental confusion change of character and manic depressive paranoid or other psychotic states are by no means rare accompaniments of heart failure They may be due to hypoxia or occasionally to hepatic failure and are encountered particularly in hypertensive of ischæmic heart failure when cerebral arteriosclerosis may be partly responsible and in severe anoxic pulmonary heart disease especially when complicated by broncho pneumonia

*Cardiac cachexia* Patients with chronic heart failure usually lose flesh although loss of weight may be prevented by fluid retention thus wasting may only be noticed after diuresis sometimes it is so great as to warrant the term cachexia Elevation of the basal metabolic rate anorexia impairment of intestinal function and enforced muscular inactivity may be partly responsible

*Venous thromboses* are common in congestive heart failure especially when the cardiac output is low They are responsible for the frequency of pulmonary infarction

*Jaundice* may develop in severe cases and may be mainly obstructive (McMichael and Sherlock 1945) or mainly hæmolytic the former depending perhaps upon the raised intra hepatic pressure the latter upon the

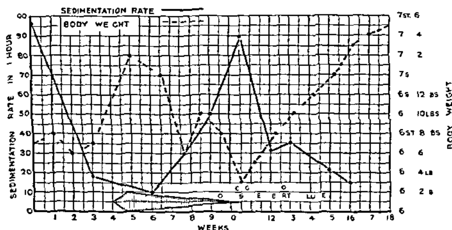



Fig 11—Fall in erythrocyte sedimentation rate resulting from the development of congestive failure in a case of active rheumatic carditis



( ) Ap l 14 1936

(b) M y 9 1936 (after treat n nt)

I g 72 —In a n n d m t f l h t u l by ong e f lu e

destruction of red cells in hæmorrhagic pulmonary infarcts The serum bilirubin is often in the region of 2 mg per cent Itching may occur

*Immature red cells* are common and may be due to stimulation of the bone marrow by anoxia Polycythæmia may be masked by hydræmia

*The erythrocyte sedimentation rate* is often retarded by congestive failure (Wood 1936) Figures of 50 to 100 in one hour obtained by the Westergren method in cases of rheumatic carditis myocardial infarction and syphilitic aortic incompetence may drop below 10 with the onset of failure and rise to their former level with recovery (fig 7 11)

*The basal metabolic rate* is usually raised by about 20 per cent in heart failure as first pointed out by Peabody *et al* (1916) A 10 per cent increase could be due to a great increase of heart weight, for a 300 Gm heart consumes about 20 to 25 ml of oxygen per minute and a failing 600 Gm heart about 50 ml of oxygen per minute (Bing *et al* 1949) The discrepancy has been attributed to extra work performed by the muscles of respiration (Resnik and Friedman 1935)

*Radiographic appearances* The transverse diameter of the heart is increased by 1 to 2 cm during failure (figs 7 12a and b) In making such measurements care must be taken to exclude apparent enlargement due to raising of the diaphragm by an enlarged liver so that the heart takes up a more horizontal position The superior vena cava throws a denser shadow than usual and the right atrium is more prominent The lesser fissure on the right side may be clearly marked owing to pleural congestion or hydrothorax may be evident

*Behaviour of the blood pressure* The blood pressure might be expected to fall in congestive heart failure but in fact it may rise fall or remain stationary in the majority of cases it rises There are only two conditions in which heart failure is characteristically associated with a sharp drop of blood pressure acute myocardial infarction and massive pulmonary embolism Conspicuous lowering of the blood pressure associated with heart failure in other diseases is commonly a terminal event The vasoconstriction that maintains the blood pressure when the cardiac output falls is partly reflex and perhaps partly renal in origin It may be recognised clinically by cold extremities and peripheral cyanosis An increased concentration of renin has been found in blood samples obtained from the renal vein in cases of congestive heart failure (Merrill Morrison and Brannon 1946) A powerful pressor agent must be at work to raise the blood pressure in the face of a cardiac output that may be only half the normal resting level In advanced heart failure impairment of hepatic function may lower the blood pressure (Raaschou 1954)

*Character of the heart sounds* Current terminology still includes such expressions as weak faint or distant heart sounds and tic tac or fœtal rhythms which have been supposed to signify failure or threatened failure Apart from cases of coronary thrombosis, pulmonary embolism and pericardial effusion, weak, faint, or distant heart sounds are commonly due to

obesity, emphysema or well developed thoracic muscles It is doubtful whether tic tac or fœtal rhythm is in any way associated with central heart failure on the other hand it is heard in patients suffering from shock and may be associated with diminution of the blood volume A weak first heart sound associated with a normal second sound is usually due to a P R interval around 0 21 to 0 22 second the mitral cusps then having time to float into apposition before the ventricles contract (Levine 1948)

## *PHYSIOLOGICAL TESTS FOR CONGESTIVE HEART FAILURE*

Although as a rule there are good clinical grounds for being confident whether heart failure is present or not difficulties arise occasionally the following tests may then be enlisted

*Valsalva manœuvre*

The diastolic hypertension and secondary bradycardia that follow strain in normal individuals are attributed to reflex vasoconstriction from stimulation of carotid and aortic baroreceptors by the diminished stroke output and pulse pressure that follow reduction of the effective filling pressure (fig 5 06) In heart failure however the overloaded ventricle maintains a normal or even increased stroke volume and pulse pressure when its filling pressure is reduced so that the baroreceptors are either not stimulated at all or respond to the increased pulse pressure by causing vasodilatation and a corresponding fall in diastolic pressure (Sharpey Schafer 1955) The square wave in figure 7 13 is due simply to the rise in all

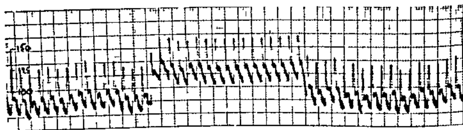


Fig 7 13—Arterial pressure pulse during Valsalva s manœuvre in a case of congestive heart failure showing a square wave effect (see text)

pressures (venous intracardiac pulmonary systemic and of course intrathoracic) that occurs during the period of strain there is no decrease of pulse pressure no diastolic hypertension no overshoot and no secondary bradycardia It is easy enough to note the effect of strain on the pulse pressure and pulse rate at the bedside so the test should have considerable clinical value

*Forearm blood flow*

A second indirect method of determining whether or not the cardiac output rises in response to an increased or decreased venous filling

pressure is to measure the forearm blood flow when the body is horizontal and when it is tilted legs down at an angle of 45 degrees or 60. In normal subjects the cardiac output rises in the horizontal position and falls in the tilted (legs down) position in response to well known postural changes in venous filling pressure and there are corresponding changes in forearm blood flow which receives its share of the output. In other words when the subject lies flat the forearm flow rises and when he is tilted legs down it falls. In patients with heart failure however the forearm blood flow responds paradoxically to changes of posture in view of the changed relationship of venous pressure to output when either ventricle is overloaded (Brigden and Sharpey Schafer 1950). This test might have clinical value if the changes in forearm flow could be detected by means of a skin temperature thermometer or photoelectric cell (recording digital pulsation).

*Direct measurement of intracardiac pressures and cardiac output*

Cardiac catheterisation makes it possible to measure both atrial pressures right ventricular diastolic pressure and cardiac output more or less at the same time. In congestive heart failure all these pressures are raised (fig. 7 14) the arterio venous oxygen difference is over 50 ml per litre

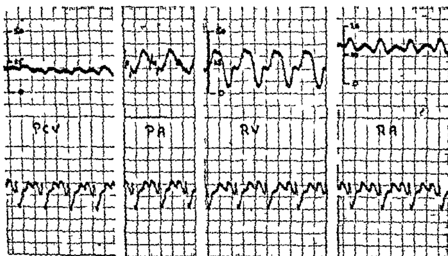



Fig. 7 14—Elevated pressures in both atria in a case of congestive heart failure involving both ventricles

the cardiac output less than 4 5 litres per minute at rest and the cardiac index (C O per square metre of body surface) below 3. In pure right ventricular failure the findings are similar except that the left atrial pressure is normal. If the patient is tilted about 45 degrees legs down or if venous tourniquets are applied to the thighs the right atrial pressure falls and the cardiac output rises in accordance with Starling's law. On effort

the A V difference increases greatly the output little if at all despite a considerable *rise of right atrial pressure and tachycardia*

## PROGNOSIS OF HEART FAILURE

When left ventricular failure develops in the natural course of hyper tensive or aortic valve disease the prognosis in untreated cases is poor patients seldom living more than eighteen months after the onset of orthopnœa or paroxysmal cardiac dyspnœa but few die before clinical signs of chronic systemic congestion become apparent Modern treatment *however has greatly improved the prognosis of left ventricular failure* particularly in hypertensive heart disease and aortic stenosis and life may be prolonged for years

The natural prognosis may be less unfavourable when acute myocardial infarction is responsible because if the patient survives the acute phase he may make a good recovery and although the average life expectancy is still only about 5 years the chances of much longer survival are not remote

The outlook is entirely different when left ventricular failure complicates acute nephritis here complete recovery may be anticipated The ultimate prognosis depends upon the subsequent course of the nephritis Similar remarks apply to other forms of hypertension which are transient or which can be treated successfully

The prognosis of right ventricular failure or congestive heart failure depends very much upon its cause When associated with diseases that can be cured or improved such as mitral stenosis or thyrotoxicosis the outlook is excellent On the other hand when it occurs in the natural course of chronic and incurable heart disease few patients survive more than a year or two Between these extremes are cases of incurable heart disease in which failure is precipitated by some adverse factor which is either transient or which can be improved or cured Undue physical work pregnancy infection disturbances of rhythm and pulmonary embolism provide examples of such factors

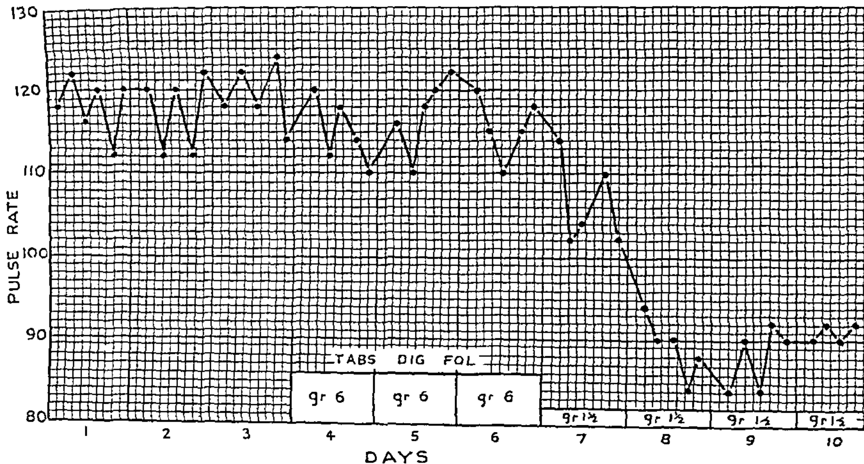
## TREATMENT

*Since the measures used in the treatment of left and right ventricular* failure are practically the same they will be considered together

Rest in bed or in a comfortable armchair is essential and should be con tinued for a minimum period of three weeks If signs of failure do not disappear within a few days of instituting adequate therapy the period of rest should be extended to six weeks The patient should be nursed against a back rest at an angle of about 60 degrees whether orthopnœic or not for there is no easier way of lowering the right atrial pressure and so unloading the overburdened heart if the legs are lowered so much the better —hence the value of an armchair or cardiac bed *Meals* should be small in quantity and fluids limited to about two pints daily If the *sodium intake*

Fig 7 15—Typical effect of digitalis on the venous pressure or right atrial pressure in four cases of congestive heart failure

Fig 7 16—Typical effect of digitalis on the blood pressure pulse rate right atrial pressure and cardiac output in a case of hypertensive heart failure with normal rhythm


ACUTE RHEUMATIC CARDITIS
CONGESTIVE HEART FAILURE
PULSE RATE
130
120
110
100
90
80
TABS DIG FOL
gr 6
gr 6
gr 6
gr 1½
gr 1½
gr 1½
gr 1½
1
2
3
4
5
6
7
8
9
10
DAYS

can be limited to 0 5 G daily however there is no need to restrict fluids Correct treatment of heart failure usually serves as the best hypnotic but if insomnia is troublesome at first there should be no hesitation in using powerful sedatives

*Venesection* deserves a better reputation It has fallen out of favour because similar results may be obtained by means of certain drugs, but it offers a quick and sure way of lowering the venous pressure and should not be abandoned About 600 to 750 ml of blood may be withdrawn

*Digitalis* obtained from the common foxglove and discovered to be a cure for cardiac dropsy by William Withering in 1785 is beneficial whether there is auricular fibrillation or normal rhythm and whether the pulse rate is fast or slow It lowers the venous pressure (fig 7 15) raises the blood pressure (fig 7 16) slows the heart rate (fig 7 17) relieves hepatic distension (fig 7 09) increases the vital capacity shortens the pulmonary circulation time (fig 7 18) increases the cardiac output (fig 7 16) and encourages diuresis (fig 7 19) Its good effects cannot be attributed to a direct venous pressure lowering action as suggested by McMichael and Sharpey Schafer (1944) for digitalis does not lower a raised venous pressure in the absence of heart failure (fig 7 20 from Wood and Paulett 1949) and in cases of left ventricular failure it raises the output reduces

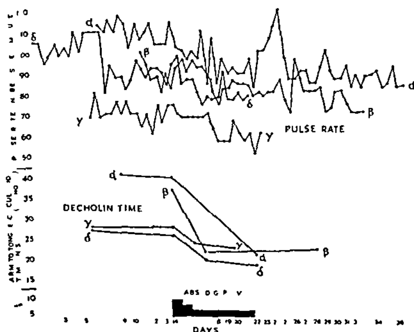



Fig 7 18—The action of digitalis on the arm to-tongue circulation time and on the pulse rate in four cases of left ventricular failure with normal rhythm

passive pulmonary hypertension and therefore lowers left atrial pressure without altering the normal right ventricular diastolic pressure (Harvey *et al* 1949) The original belief that digitalis improves the function of the heart by virtue of its direct action on the myocardium is probably correct In normal controls increase of myocardial tone may make the heart smaller and may reduce its output (Stewart *et al* 1938)

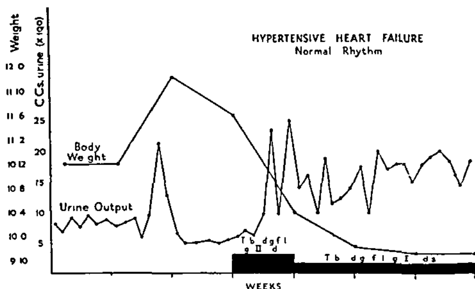



Fig 7 19—Chart showing considerable diuresis resulting from the administration of digitalis to a case of hypertensive heart failure with normal rhythm

Digitalis should not be withheld when heart failure is due to cardiac ischæmia, cor pulmonale or heart block

In ischæmic heart disease digitalis was believed to be dangerous because it was shown to encourage ventricular tachycardia or fibrillation in cats subjected to experimental cardiac infarction (e g Travell Gold and Modell 1938) and because the microscopic myocardial lesions caused by digitalis in cats (Buchner 1934) closely resembling those produced by acetylcholine and prolonged vagal stimulation (Hall *et al* 1937) were likewise attributed to coronary vasoconstriction because they could be prevented by means of coronary vasodilators such as aminophylline (Kyser Ginsberg and Gilbert 1946) and because digitalis is known to have a cholinergic action (Danielopolu 1946) But in clinical practice digitalis in therapeutic doses has no effect whatever on the severity duration or frequency of attacks of angina pectoris (Gold *et al* 1938) and both digitalis and ouabain have proved efficient treatment for cardiogenic shock following acute cardiac infarction (Gorlin and Robin 1955) as well as for ordinary ischæmic heart failure Finally Bing *et al* (1950) have proved that strophanthus has no effect on coronary blood flow

Fig. 7 26—Chart illustrating the failure of digitalis to lower the right atrial pressure in twelve cases in which it was raised from causes other than congestive failure

Digitalis tended to be withheld in cases of cor pulmonale when a raised venous pressure was associated with signs of a raised cardiac output because Howarth McMichael and Sharpey Schafer (1947) had shown that the high output (which was compensatory and beneficial) fell if the venous pressure was lowered (by venesection for example) and at that time these workers believed that digitalis was a primary venous pressure lowering agent moreover digitalis seemed to be of little value clinically unless the cardiac output was obviously low The hypothesis that digitalis is a primary venous pressure lowering agent has since been abandoned (McMichael 1952) and it is now generally believed that digitalis is beneficial in cor pulmonale if there is true heart failure but not otherwise it may certainly be tried, however, without fear of harming the patient

It is doubtful if there are any real contra indications to digitalis in therapeutic doses The suggestion that it encouraged thrombosis has been refuted (Cathcart and Blood 1950) Potassium depletion appears to make the heart hypersensitive to digitalis (Friedman and Bine 1948 Lown *et al* 1951) Peptic ulcers and other disorders of the gut that react unfavourably to cholinergic agents may be aggravated by digitalis

For routine purposes the dose of digitalis should be 3 grains (0 2 G) *of the powdered leaf t d s on the first day 2 grains (0 13 G) t d s on the* second and 1 grain (65 mg) t d s thereafter until demonstrable improvement or evidence of intoxication occurs when it may be reduced to 1 grain (65 mg) b i d Heavy loading doses should only be given when it is known that the patient has received no digitalis for at least one month Other methods of administering digitalis are described on page 255

Strophanthin may be preferred when a quick action is desired especially if a cumulative effect is not wanted A single dose of Ouabain 1 0 mg intravenously may raise the cardiac output in cases of heart failure without affecting the venous pressure (McMichael 1948) and so presumably acts directly on the heart Like intravenous digoxin it also has a conspicuous pressor effect and slows the pulse rate Strophanthin may be the drug of choice in collapsed cases of cor pulmonale

*Mercurial diuretics* were discovered more or less by accident at the Wenckebach clinic in Vienna in 1919 when it was noticed that a new *anti* syphilitic mercurial substance novasurol *when injected into a de*hydrated young girl with congenital syphilis provoked unexpected diuresis (Vogl 1950) Novasurol however was painful and toxic and was soon replaced by the more potent yet more benign salyrgan (Bernheim 1924) *Theophylline was combined with the organic mercurial component in 1928* (von Issekutz and von Vegh) in the hope that a summation effect would increase the diuresis but the combination introduced as novurit proved less painful and more effective than expected being better absorbed and more efficiently excreted owing to a *fundamental* change in the structure of the substance when theophylline was incorporated (de Graff Batterman and Lehman 1938) This is the basis of mersalyl (B P) modern salyrgan

(Bayer) neptal (M & B) esidrone (Ciba) and the American mercurophylline and mercuhydrin All these substances contain about 40 per cent of metallic mercury ampoules for injection contain 10 per cent of the drug and 5 per cent of theophylline The usual dose is 2 ml intramuscularly which contains 80 mg of metallic mercury and 0 1 Gm of theophylline It may be repeated every third or fourth day preferably with ammonium chloride gr. 30 t d s on the day of the injection to replace chloride loss

In mercaptomerin (thiomerin) the organic mercurial substance is combined with a mercaptide group instead of theophylline this has greatly decreased toxicity while preserving full diuretic potency moreover thiomerin may be given subcutaneously for it causes very little local irritation and is therefore practically painless (Batterman *et al* 1949)

From time to time attempts have been made to encourage oral mercurial diuretics but in the past they have never withstood prolonged clinical trials being too irritating to the gastric mucosa and too inefficient The latest is merchloran (chlormerodrin) in a dose of 2 tablets each equivalent to 10 mg of mercury three or four times a day (Moyer *et al* 1952) With these doses however gastro intestinal symptoms are frequent and as a rule only 1 tablet is given three or four times daily at the start and once or twice daily for maintenance

Mersalyl rectal suppositories which contain 0 4 Gm of mersalyl and 0 2 Gm of theophylline usually provoke severe local burning pain and cannot be recommended

Mercurial diuretics act by discouraging tubular reabsorption of sodium potassium and chloride (Blumgart *et al* 1934) and so remove œdema in water logged patients and cause dehydration in those without œdema (De Vries 1946) The blood volume declines and the venous pressure falls secondarily If the heart is overloaded the cardiac output rises and the whole functional state of the circulation improves These effects are gradual beginning an hour or two after the injection and depend upon the degree of diuresis (Volini and Levitt 1939) A much earlier and more rapid fall of venous pressure may result from the incorporated theophylline (Pugh and Wyndham 1949) If the right ventricle is not overloaded its output probably falls and this helps to decongest the lungs in cases of left ventricular failure or mitral stenosis (Friedman *et al* 1935) Thus mersalyl has proved an excellent drug for preventing paroxysmal cardiac dyspnœa (fig 7 21)

Toxic reactions are rare but high fever and rigors have been encountered (Foster and Naylor 1951)

Sudden death has been reported after intravenous injections This is a direct toxic effect of a relatively high concentration of mercury on the heart death occurring from ventricular fibrillation or asystole within 1 to 3 minutes of the injection It may occur after the first injection, when previous injections seem to have been well tolerated or after warnings of disaster have been noted on previous occasions (Kaufman 1948) Sudden

death of this kind is very rare after intramuscular or subcutaneous injections. Ventricular fibrillation or asystole however may also occur after a massive diuresis. it has been suggested that the combination of potassium depletion (which sensitises the heart to digitalis) and digitalis concentration may be responsible.

Considerable weakness and fatigue may follow the use of mercurial diuretics and have been attributed to sodium potassium and chloride depletion the feeling of exhaustion occurs especially the day after the

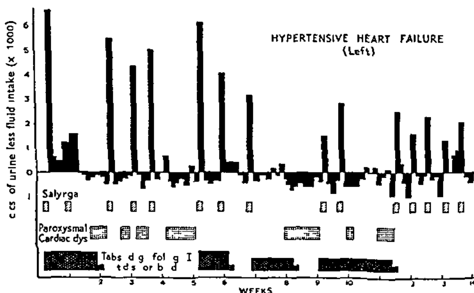



Fig 7 21—Chart illustrating the beneficial effect of mercurial diuretics in preventing paroxysmal cardiac dypsnœa Digitalis was less effective

injection and is only partly relieved by potassium and chloride Nausea and vomiting colic or diarrhœa may be due to digitalis concentration An attack of gout may be precipitated by the dehydration in susceptible individuals Patients with prostatic symptoms may develop acute retention as a result of distension of the bladder and should be warned to void urine hourly after an injection without waiting for the desire Abdominal cramps are due to sodium depletion Hiccough and drowsiness suggest uræmia and usually mean that treatment has been too intense and that the blood sodium and chloride are too low This is rare unless the patient is also on a low sodium diet

Toxic nephrosis, characterised by tubular degeneration and calcification is encountered occasionally usually after prolonged administration (Waife and Pratt 1946)

The drug should not be stopped owing to a poor initial response for the result of the second or third dose coinciding perhaps with the beneficial

effect of rest and digitalis may exceed expectations The only contra indications are known hypersensitivity and acute nephritis

*Other diuretics* *Mictine* in doses of 200 to 600 mg t d s for two consecutive days each week is the most powerful oral diuretic now available and is usually well tolerated Of the xanthines *theobromine* 0 5 G is the most potent it is best given in the form of 1 0 G of diuretin (theobromine and sodium salicylate) which is more soluble

*A low sodium diet* has proved a most effective way of relieving obstinate œdema (Schroeder 1941) and preventing paroxysmal cardiac dyspnœa The object is to reduce the sodium intake to the order of 0 5 G daily so that it is impossible for the tissues to hold much fluid The blood volume is thus reduced and the venous pressure lowered The function of the overloaded heart improves as it does after venesection Both the milk diet of Karell (1866) and the rice diet of Kempner (1944 1946) owe their diuretic effects to their low sodium content

The following diet has been constructed from tables giving the com position of numerous foods compiled by McCance and Widdowson (1946) The first figure after each substance gives the amount of sodium in mgs per 100 G of foodstuff The second figure gives the approximate calorific value of the food per mg of sodium content Obviously the best foods are those with a low first figure and a high second figure For the first 48 hours it is a good plan to give nothing but fruit in any form, fruit juice drinks sugar rice and diluted milk Mercurial diuretics should not as a rule be given more than two or three times with this diet the combination causing too much sodium and chloride depletion uræmia which may prove fatal may then develop (Shroeder 1949 Black and Litchfield 1951)

## LOW SODIUM DIET

### CEREALS

| *Permitted* | | | *Doubtful* | | | *Forbidden* | | |
|---|---|---|---|---|---|---|---|---|
| Arrowroot | 4 8 | 72 | Currant bread | 164 | 2 | Bread | 393 | 0 7 |
| Barley | 0 8 | 150 | Sweet biscuits | 216 | 3 | Biscuits | 400 | 0 8 |
| Cornflour | 52 | 7 | Rusks | 200 | 2 | Cornflakes | 1 050 | 0 3 |
| Flour | 2 5 | 170 | | | | Grapenuts | 658 | 0 5 |
| Macaroni | 7 9 | 15 | | | | Post Toasties | 810 | 0 5 |
| Oatmeal | 33 | 11 | | | | Ryvita | 615 | 0 5 |
| Rice | 2 | 60 | | | | Vita weat | 615 | 0 5 |
| Sago | 3 4 | 100 | | | | | | |
| Semolina | 12 | 30 | | | | | | |
| Shredded Wheat | 16 | 22 | | | | | | |
| Tapioca | 4 | 86 | | | | | | |

NOTE

*Biscuits* Water biscuits and cream crackers contain the most sodium Oatmeal biscuits made without salt and with lard instead of margarine are recommended

*Breakfast cereals* Oatmeal porridge should be made without salt and with

equal parts of milk and water Shredded wheat with diluted milk and plenty of sugar is recommended

*Milk puddings* Milk should be diluted with equal parts of water margarine must not be used

*Flour sauces* Make without salt and with equal parts of milk and vegetable water Use dripping instead of margarine

*Bread* Home made bread made with yeast flour lard and milk without salt is allowed

### Dairy Produce and Fats

| *Permitted* | | | *Doubtful* | | | *Forbidden* | | |
|---|---|---|---|---|---|---|---|---|
| Butter (fresh) | 223 | 3 5 | Milk (fresh) | 50 | 1 2 | Cheese | 600 | 0 5 |
| Cream cheese (home made) | 110 | 8 | Milk (sweet condensed) | 143 | 2 | Egg white | 192 | 0 2 |
| Cream | 31 | 13 | | | | Margarine | 318 | 0 5 |
| Egg yolk | 50 | 7 | | | | Butter (salted) | | |
| Olive oil | 0 1 | 9 -90 | | | | | | |
| Lard | 2 | 450 | | | | | | |
| Dripping | 5 | 00 | | | | | | |
| Suet | 25 | 44 | | | | | | |

NOTE

Butter may be kneaded in water to reduce its salt content

Home made cream cheese must be made without salt

Dilute milk with half its volume of water

Use olive oil dripping lard or suet in cooking instead of butter or margarine whenever possible

### Meat Poultry and Game

| *Permitted* | | | *Doubtful* | | | *Forbidden* | | |
|---|---|---|---|---|---|---|---|---|
| Roast beef | 6 | 6 | Chicken | 80 | 2 | Bacon | 1 200 | 0 3 |
| Grilled steak | 67 | 5 | Duck | 195 | 1 5 | Beef (silverside) | 1 470 | 0 2 |
| Stewed steak | 38 | 5 5 | Goose | 145 | 2 | Brains | 150 | 0 7 |
| Hare (roast or stewed) | 45 | 4 5 | Guinea fowl | 136 | 1 5 | Ham | 1 500 | 0 3 |
| Mutton chop (grilled or fried) | 90 | 6 | Heart | 153 | 1 5 | Kidney | 250 | 0 4 |
| Mutton leg etc (roast boiled or stewed) | 68 | 4 | Liver | 100 | 2 5 | Meat paste | 940 | 0 25 |
| Pork roast | 66 | 5 | Partridge, Pheasant, Pigeon | 100 | 2 | Smoked pork | 1 800 | 0 15 |
| Pork chops | 60 | 9 | Turkey | 130 | 1 5 | Sausage | 1 000 | 0 25 |
| Rabbit | 32 | 6 | Tripe | 72 | 1 5 | Tongue (preserved) | 1 870 | 0 15 |
| Sweetbread | 69 | 3 | Veal | 100 | 2 | | | |
| Tongue (fresh) | 79 | 4 | Venison | 86 | 2 | | | |
| Topside (beef) | 50 | 4 | | | | | | |

NOTE

All salted and preserved meats are forbidden

Roasts are best since they contain more calories per mg of sodium content

Meat extracts like Bovril and Oxo are forbidden

The simple meats – beef mutton lamb pork hare and rabbit – are the best Next comes game Of offal sweetbread fresh tongue and liver are best

## Fish

| *Permitted* | | |
|---|---|---|
| Bass | 75 | 1 7 |
| Brill (steamed) | 94 | 1 - |
| Dabs (fried) | 127 | 2 0 |
| Eels (stewed) | 73 | 5 1 |
| Herring (fried) | 101 | 2 3 |
| Herring s roe fre h (fried) | 87 | 3 0 |
| Mullet | 94 | 1 3 |
| Plaice (fried) | 124 | 1 9 |
| Salmon (fresh) | 107 | 1 9 |
| Sprats (fried) | 132 | 3 4 |
| Trout fre h wat r | 88 | 1 5 |
| Turbot | 90 | 1 1 |

| *Doubtful* | | |
|---|---|---|
| Bream (sea) | 113 | 0 88 |
| Cod fried | 161 | 0 87 |
| grilled | 110 | 1 5 |
| steamed | 100 | 0 82 |
| Cod s roe (fried) | 127 | 1 6 |
| Flounder (steamed) | 115 | 0 83 |
| Haddock (steamed) | 121 | 0 80 |
| Hake (steamed) | 118 | 0 90 |
| Hake (fried) | 153 | 1 3 |
| Halibut | 110 | 1 2 |
| Mackerel (fried) | 153 | 1 2 |
| Plaice (steamed) | 120 | 0 77 |
| Pollack (steamed) | 95 | 0 91 |
| Pollack (fried) | 162 | 0 96 |
| Skate (fried) | 182 | 1 3 |
| Sole Do er (fried) | 192 | 1 2 |
| Sole Dover (steamed) | 110 | 0 76 |
| Sole lemon (fried) | 136 | 1 6 |
| Sole lemon (steamed) | 115 | 0 78 |
| Whiteba t (fried) | 225 | 2 4 |
| Whiting | 127 | 0 71 |

| *Forbidden* | | |
|---|---|---|
| Bloaters | 703 | 0 36 |
| Cockles | 3 5 0 | 0 01 |
| Crab (boiled) | 366 | 0 35 |
| Fish paste | 1,480 | 0 12 |
| Haddock (smoked) | 1 2-0 | 0 08 |
| Kippers | 990 | 0 08 |
| Lobster | 325 | 0 36 |
| Mussels (boiled) | -10 | 0 41 |
| Oysters | 505 | 0 10 |
| Prawns | 1 590 | 0 06 |
| Scallops | 265 | 0 4 |
| Shrimps | 3 840 | 0 03 |
| Trout (sea) | 207 | 0 63 |
| Whelks | 265 | 0 34 |
| Winkles (boiled) | 266 | 0 37 |

NOTE

Fish cakes made with any but forbidden fish without salt and fried in olive oil are recommended

## Fruit

| *Permitted* | | |
|---|---|---|
| Apples | 2 | 20 |
| Apricots | 1 | 30 |
| Bananas | 1 2 | 70 |
| Blackberries | 3 7 | 8 |
| Cherries | 2 8 | 16 |
| Currants | 2 7 | 10 |
| Dates | 4 7 | 27 |
| Figs | 1 6 | 26 |
| Gooseberry | 1 - | 31 |
| Grapes | 1 6 | 40 |
| Grape fruit | 1 4 | 16 |

| *Permitted* | | |
|---|---|---|
| Greengages | 1 4 | 34 |
| Oranges | 2 9 | 9 |
| Peaches | 2 7 | 13 |
| Pears | 2 3 | 18 |
| Pineapple | 1 7 | 29 |
| Plums | 1 7 | 2- |
| Quinces | 3 2 | 8 |
| Raspberries | - 5 | 10 |
| Rhubarb | 1 5 | 2 5 |
| Strawberries | 1 5 | 17 |

NOTE

These are average samples of fresh fruits

Doubtful fruits are melon (19 5/1) and passion fruit (30/1)

Stewed fruit is best because of its higher calorific value e g stewed apples (0 1/170)

Tinned fruits in syrup are also good

Dried fruits are less beneficial e g tinned apricots (0 9 62) dried apricots (56/3) Raisins and sultanas at 52/4 7 may be allowed occasionally

Preserved olives (2 250/0 05) are forbidden

equal parts of milk and water Shredded wheat with diluted milk and plenty of sugar is recommended

*Milk puddings* Milk should be diluted with equal parts of water margarine must not be used

*Flour sauces* Make without salt and with equal parts of milk and vegetable water Use dripping instead of margarine

*Bread* Home made bread made with yeast flour lard and milk without salt is allowed

### Dairy Produce and Fats

| *Permitted* | | | *Doubtful* | | | *Forbidden* | | |
|---|---|---|---|---|---|---|---|---|
| Butter (fresh) | 223 | 3 5 | Milk (fresh) | 50 | 1 [illegible] | Cheese | 600 | 0 5 |
| Cream cheese | | | Milk (sweet | | | Egg white | 192 | 0 2 |
| (home made) | 110 | 8 | condensed) | 143 | 2 | Margarine | 318 | 0 5 |
| Cream | 31 | 13 | | | | Butter (salted) | | |
| Egg yolk | 50 | 7 | | | | | | |
| Olive oil | 0 1 | 9 290 | | | | | | |
| Lard | [illegible] | 450 | | | | | | |
| Dripping | 5 | 200 | | | | | | |
| Suet | 25 | 44 | | | | | | |

NOTE

Butter may be kneaded in water to reduce its salt content

Home made cream cheese must be made without salt

Dilute milk with half its volume of water

Use olive oil dripping lard or suet in cooking instead of butter or margarine whenever possible

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| Grilled steak | 67 | 5 | Duck | 195 | 1 5 | Beef | | |
| Stewed steak | 38 | 5 5 | Goose | 145 | 2 | (silverside) | 1 470 | 0 2 |
| Hare (roast or | | | Guinea fowl | 136 | 1 5 | Brains | 150 | 0 7 |
| stewed) | 45 | 4 5 | Heart | 153 | 1 5 | Ham | 1 500 | 0 3 |
| Mutton chop | | | Liver | 100 | 2 5 | Kidney | [illegible]50 | 0 4 |
| (grilled or | | | Partridge | | | Meat paste | 940 | 0 25 |
| fried) | 90 | 6 | Pheasant | 100 | 2 | Smoked pork | 1 800 | 0 15 |
| Mutton leg etc | | | Pigeon | | | Sausage | 1 000 | 0 25 |
| (roast boiled | | | Turkey | 130 | 1 5 | Tongue | | |
| or stewed) | 68 | 4 | Tripe | 72 | 1 5 | (preserved) | 1 870 | 0 15 |
| Pork roast | 66 | 5 | Veal | 100 | 2 | | | |
| Pork chops | 60 | 9 | Venison | 86 | 2 | | | |
| Rabbit | 32 | 6 | | | | | | |
| Sweetbread | 69 | 3 | | | | | | |
| Tongue (fresh) | 79 | 4 | | | | | | |
| Topside (beef) | 50 | 4 | | | | | | |

NOTE

All salted and preserved meats are forbidden

Roasts are best since they contain more calories per mg of sodium content

Meat extracts like Bovril and Oxo are forbidden

The simple meats – beef mutton lamb pork hare and rabbit – are the best Next comes game Of offal sweetbread fresh tongue and liver are best

Honey (10 7/26) and jam (15 9/16) are recommended

Golden syrup (270/1) chutney (150/1) and mincemeat (200/0 5) are prohibited

*Toffee (115/3 5) and black treacle (96/2 5) should be avoided*

### Beverages

| *Permitted* | | | *Prohibited* | | |
|---|---|---|---|---|---|
| Coffee | 0 3 | 15 | Bournvita | 360 | 1 |
| Lemonade | 0 5 | 100 | Bovril | 5 580 | 0 02 |
| Tea | 0 4 | 2 | Cocoa | 650 | 0 7 |
| Beer | 15 | 3 | Horlicks | 690 | 0 6 |
| Wine | | | Marmite | 6 130 | 0 01 |
| Spirits | | | Ovaltine | 249 | 1 5 |
| | | | Oxo Cubes | 10 600 | 0 02 |
| | | | Virol | 374 | 1 |

### Condiments

| *Permitted* | | | *Prohibited* | | |
|---|---|---|---|---|---|
| Ginger | 34 | 7 5 | Curry | 450 | 0 5 |
| Mustard | 5 | 90 | Salt | 38 500 | 0 |
| Pepper | 7 | 45 | | | |
| Vinegar | 20 | 0 2 | | | |

NOTE

Since so small a quantity of curry is required to flavour a dish it may be allowed despite the adverse figures shown

### Cakes Pastries and Puddings

| *Permitted* | | | *Doubtful* | | | *Forbidden* | | |
|---|---|---|---|---|---|---|---|---|
| Apple dishes | 50 | 4 | Biscuits | 150 | 3 | Cakes | 150–500 | 2–3 |
| Blancmange | 45 | 2 5 | Buns | 120 | 3 | | | |
| Cereal puddings (rice etc ) | 50 | 3 | Cheese cake | 138 | 3 | Dumpling | 488 | 0 5 |
| | | | Jam roll | 151 | 2 5 | Gingerbread | 336 | 1 |
| Custard | 50 | 2 | Rock cakes | 150 | 3 | Mince pies | 225 | 1 5 |
| Doughnuts | 60 | 6 | Tarts | 150 | 3 | Pastries | 250 | 2 |
| Fruit custard | 30 | 3 | | | | Puddings | 100–250 | 1–3 |
| Fruit tarts | 76 | 3 | | | | | | |
| Jelly | 8 | 9 5 | | | | Scones | 170 | 2 |
| Milk jelly | 33 | 3 | | | | Swiss roll | 650 | 0 4 |
| Pancake | 88 | 4 | | | | Yorkshire pudding | 412 | 0 5 |
| Shortbread | 86 | 6 | | | | | | |
| Sponge cake | 79 | 4 | | | | | | |
| Trifle | 50 | 3 | | | | | | |

NOTE

Oatmeal biscuits are allowed if made without salt and with lard instead of butter or margarine

Cereal puddings should be made with diluted milk and without margarine

Yorkshire pudding is permissible if made without salt

### General Rules

No free salt or ordinary salt substitutes no salt in cooking Sodium free salt substitutes usually made with potassium such as neo seleron are permitted

No foods made with baking powder

No medicines containing sodium

No preserved salted smoked or tinned foods (except dried and tinned fruit)

Dilute milk with half its volume of water

Use dripping lard olive oil or suet instead of butter or margarine wherever possible

Supply calories chiefly with selected cereals cream fat fresh meat, potatoes sugar sweets fruit and nuts

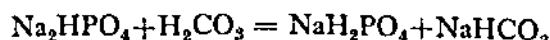
Avoid bread biscuits certain cereals margarine salted butter cheese bacon ham tongue sausages meat extracts shell fish fish paste milk beverages cakes and pastries

Fluid should be encouraged but few patients feel like drinking much if they are adhering to the diet faithfully

*Cation exchange resins* are synthetic insoluble macromolecular organic compounds in powder form which when suspended in a solution behave like electrolytes acid resins exchange hydrogen ions for any other cation in the solution but prefer calcium potassium or sodium in that order In 1946 Dock pointed out that such resins would absorb sodium from the gut and since then they have gradually found their place as adjuncts to the mercurial diuretics and the low sodium diet (Dock and Frank 1950) At the present time the most effective and readily available cation exchange resin for therapeutic purposes is probably carbo resin (Lilly) Two thirds of the 88 per cent cation exchange fraction of this resin is in the carboxylic acid form one third in the form of its potassium salt In the human gut each gramme of carbo resin is capable of absorbing 1 meq (23 mg) of sodium and passing it out in the fæces when the patient is taking about 1 5 Gm of sodium per day If the dose is 15 Gm suspended in water three times a day 1 Gm of sodium should be removed daily in this way The amount of sodium absorbed by the resin is proportional to the quantity of sodium in the diet Thus with a 0 5 Gm low sodium diet 1 Gm of resin absorbs only 0 3 meq of sodium on a 3 Gm low sodium diet it may absorb as much as 2 meq Undue loss of potassium presents no problem with this resin but calcium deficiency may arise if treatment is prolonged As a rule, however patients do not like taking resins and they are mostly used intermittently as a protection against unavoidable or wilful dietetic indiscretions or liberties—e g while on holiday Neither potassium nor calcium should be given at the same time as the resin or it will absorb less sodium and if there is constipation which is a common complication of resin therapy, it should not be relieved by magnesium salts for the same reason

*Carbonic anhydrase inhibitors*

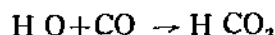
Conservation of body base and excretion of acid is partly achieved by the distal tubules where sodium alkaline phosphate interacts with carbonic acid to form acid phosphate and bicarbonate



$$Na_2HPO_4 + H_2CO_3 = NaH_2PO_4 + NaHCO_3$$

The acid phosphate is excreted and the bicarbonate reabsorbed so that half the sodium is saved This reaction is helped by an anzyme carbonic

anhydrase which accelerates the formation of carbonic acid from CO and water



$$H\ O + CO \rightarrow H\ CO_3$$

If the formation of H $CO_3$ were to be suppressed alkaline phosphate would be excreted as such and sodium would be no longer conserved

In 1940 Mann and Keilin identified sulphanilamide as a specific inhibitor of carbonic anhydrase and after further research Roblin and his colleagues found that of all the active heterocyclic sulphonamides diamox was the most promising in this respect (Miller *et al* 1950) It is rapidly absorbed and is excreted unchanged by the kidney in 6 to 12 hours A single oral dose of 250 mg is sufficient to interfere with the chain of events outlined above so that the tubules experience difficulty in reabsorbing sodium

In clinical practice however diamox in doses of 250 mg daily has so far proved disappointing and certainly the weakest of the four methods of relieving the body of sodium

*Combined low sodium regime*

With these four weapons adequate control of the sodium balance is not at all difficult The art is to find the best combination for each particular patient and the danger is the low salt syndrome first described by Shroeder (1949) The most powerful of the four is the diet and if patients will only abide by it absolutely the other three methods may usually be withheld altogether moreover patients tend to lose their taste for salt if they resolutely refuse to titillate it If patients prefer a 2 or 3 Gm sodium diet they will certainly need weekly injections of mersalyl or thiomerin daily merchloran if they can tolerate it or fairly heavy doses of a potent cation exchange resin diamox alone is rarely strong enough to hold the situation in check Patients who do not mind the diet for the most part but who insist on occasional breaks can have these lapses adequately covered by a mercurial diuretic or resin

The low sodium regime has revolutionised the treatment of heart failure and is a great deal more effective than digitalis except in cases of auricular fibrillation with rapid ventricular rate It is also just as successful in isolated left ventricular failure as in congestive heart failure or pure right ventricular failure It has the triple value of combatting œdema itself reducing the blood volume and venous pressure and so improving the function of the overloaded heart and relieving pulmonary venous congestion whether due to heart failure or mitral stenosis

*Aminophylline*

Aminophylline (theophylline ethylenediamine) benefits cases of heart failure in four different ways (1) It lowers the venous pressure promptly and thereby relieves both left and right ventricular failure (2) it is an excellent bronchial antispasmodic and therefore particularly helpful in

cor pulmonale (3) it is a powerful respiratory stimulant acting reflexly by way of carotid sinus chemoreceptors and abolishes Cheyne-Stokes breathing as first recognised by Vogl (1927 1942) (4) to some extent it appears to be a cardiac tonic, for it makes the heart beat more strongly There is no evidence that it improves the cerebral circulation (Wechsler, Kleiss and Kety 1950) and direct measurements of coronary blood flow in man by means of coronary sinus catheterisation do not support the belief that aminophylline is a coronary vaso dilator (Foltz *et al* 1950)

The drug may be given intravenously in doses of 0 25 to 0 5 Gm in cases of paroxysmal cardiac dyspnœa or pulmonary œdema with dramatic results it should be injected slowly in order to avoid overstimulating respiration Unfortunately aminophylline is often very painful when given intramuscularly owing to its high pH although preparations are on the market for use by this route

Orally aminophylline causes severe dyspepsia if given in effective doses the usual 0 1 Gm tablet three times daily after meals being far too small Some attempts have been made to overcome this difficulty perhaps the best preparation so far being theodrox (Riker) in which 0 2 Gm of aminophylline is combined with 4 gr of dried aluminium hydroxide gel taken four hourly 0 2 Gm of aminophylline is an adequate dose and theodrox is relatively well tolerated

An aminophylline suppository of 0 4 Gm at night will prevent both Cheyne Stokes breathing and paroxysmal nocturnal dyspnœa and in doing so may earn the patient s thanks for a good night s sleep

*Etophylate* a preparation in which theophylline ethanoic acid is combined with diethylenediamin (piperazine) has the great advantage of having a pH around 7 and is therefore non irritant moreover it is freely soluble and stable while retaining the therapeutic properties of theophylline It may be given orally in doses of 0 5 Gm three times daily and is painless if injected intramuscularly in similar dosage

Choline theophyllinate may also be taken by mouth in doses of 0 3 to 0 5 G t d s without fear of gastric disturbance but since the pH of a 0 8 per cent aqueous solution is 9 7 it is unsuitable for intramuscular injection

*Oxygen* is of little value in heart failure except in the following circumstances (1) in anoxic cor pulmonale (2) when acute bronchitis or bronchopneumonia has precipitated or complicated heart failure from other causes (3) in massive pulmonary embolism (4) in acute pulmonary œdema (5) in rare cases of heart failure occurring in cyanotic forms of congenital heart disease and (6) in acute cardiogenic shock from cardiac infarction

*Acupuncture* When œdema is gross and fails to respond to the measures previously outlined it may be necessary to resort to acupuncture A triangular cutting needle is used and about a dozen punctures are made in each leg the patient is then seated in a chair with his legs in a tub To facilitate drainage the legs may be swabbed down with warm citrate solution from time to time Due antiseptic precautions must be maintained Fluid

may continue to exude for twenty four to forty eight hours and it is not uncommon for the total quantity to be measured in gallons Southey s tubes constitute a cleaner way of removing fluid on the same principle Several large bore needles are inserted into the subcutaneous tissues of the thighs or calves and fluid is allowed to drain away through attached rubber tubes into a container

Relatively little protein but a lot of sodium is lost by this method and the good effect is not merely cosmetic on the contrary, the blood volume diminishes the venous pressure falls the cardiac output may pick up and spontaneous diuresis may follow

*Attacks of paroxysmal cardiac dyspnœa or of acute pulmonary œdema* are treated by methods designed to lower the venous filling pressure as quickly as possible and so to reduce the output of the right ventricle The sitting position will usually have been adopted already by the patient Morphine ¼ to ⅓ of a grain (15 to 20 mg ) intramuscularly or ⅙ of a grain (10 mg ) intravenously depresses the excited respiratory reflexes and soothes the patient Pethidine 50 to 100 mg intramuscularly may be equally effective Venous tourniquets may be applied round the thighs to trap blood in the legs or venesection may be preferred Theophylline ethylene diamine (aminophylline) 0 24 to 0 48 G intravenously lowers the venous pressure immediately relieves bronchial spasm and may have a direct stimulating action on the heart (fig 7 02) Tetraethylammonium bromide 200 to 300 mg intravenously is a useful agent for lowering venous pressure and may relieve attacks quickly (Hayward 1948) Hexamethonium bromide 20 to 30 mg or pentapyrrolidinium bitartrate (ansolysen) 5 mg subcutaneously may be equally effective

Digoxin and strophanthin are probably best avoided in view of their pressor actions indeed paroxysmal cardiac dyspnœa may occasionally be initiated by intravenous digoxin

Oxygen is of little value in paroxysmal cardiac dyspnœa for the arterial oxygen saturation is normal but may be given with advantage in acute pulmonary œdema Nikethamide is contraindicated for the aim is to depress respiration not to stimulate it Adrenaline is dangerous in ischæmic cases because it may provoke angina pectoris paroxysmal ventricular tachycardia or ventricular fibrillation but it may be given in doses of 0 5 mg subcutaneously to relieve bronchial spasm in hypertensive cases (Platz 1947) Atropine should be avoided for it has no therapeutic value and causes unnecessary tachycardia

Dramatic results may follow treatment directed against *the cause of the underlying heart disease* This applies particularly to cases of thyrotoxicosis anæmia beri beri arterio venous aneurysm severe pulmonary stenosis large patent ductus atrial septal defect mitral or aortic stenosis and primary abnormalities of rhythm and to a lesser extent to bronchitis and asthma active syphilitic aortitis bacterial endocarditis and any form of systemic hypertension

If in spite of all these measures, heart failure continues an attempt may be made to reduce the oxygen requirement and therefore the work of the heart by means of antithyroid drugs *or total ablation of the thyroid gland* (Blumgart Levine and Berlin 1933) The former is preferable because the treatment can be abandoned if unsuccessful (Bedford 1949) Relatively large doses are necessary usually 0 2 to 0 3 Gm of propyl thiouracil daily It must be admitted however that results are far from satisfactory Radioactive iodine offers another means of inducing artificial myxoedema (Blumgart *et al* 1950)

*Ligation of the inferior vena cava* below the renal veins may be tried in obstinate cases (Cossio 1952) The surgical mortality is about 6 per cent and in at least half the cases initial improvement has been maintained for months or years The operation lowers the central venous pressure Œdema tends to clear rather than increase The chief complication is recurrent phlebothrombosis in the legs

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( ) Fac es (note bilateral iridectomy)



(b) Showing h gh arched palate and deformed teeth



(c) Spider fingers

Fig 8 01—A case of arachnodactyly

This patient was 6 ft h gh and also showed hypotonia scoliosis and flat feet



Fig 8 02—Hyperteleorism in a case of pulmonary stenosis with reversed interatrial shunt

## CLASSIFICATION

It has been customary to divide congenital heart disease into acyanotic and cyanotic forms and to subdivide the latter into types with permanent cyanosis (morbus cœruleus or blue babies) and types with late terminal or transient cyanosis (cyanose tardive). This has never proved entirely satisfactory and a new classification is therefore offered It was based originally on a series of 200 proved clinical cases (Wood 1950) and takes function into account The series has since increased to 900 and the relative incidence of each type is now given in the table These figures do not apply to infants many of whom die during the first year of life

NO SHUNT

| GENERAL | per cent | LEFT SIDED | per cent | RIGHT SIDED | per cent |
|---|---|---|---|---|---|
| Dextrocardia | 0·5 | Aortic atresia | rare | Ebstein's anomaly of the tricuspid valve* | 1·0 |
| Familial cardiomegaly | rare | Aortic hypoplasia | 0·5 | | |
| Friedreich's disease | rare | Aortic incompetence | 0·5 | | |
| Gargoylism | rare | Aortic rings | rare | Idiopathic dilatation of the pulmonary artery | 1·0 |
| Heart block | 1·5 | Aortic stenosis | 3·0 | | |
| Von Gierke's disease | rare | Coarctation of the aorta | 9·0 | Pulmonary stenosis (isolated) | |
| | | Cor triatriatum | rare | infundibular | 2·0 |
| | | Fibroelastosis | rare | valvular | 10·0 |
| | | Left coronary artery arising from pulmonary artery | rare | | |
| | | Mitral stenosis | rare | | |
| | | Right sided aortic arch (isolated) | rare | | |
| Total | 2·0 | Total | 13·0 | Total | 14·0 |

* Some cases are cyanotic

| WITH SHUNT | | | |
|---|---|---|---|
| ACYANOTIC<br>LEFT TO RIGHT SHUNT<br>(pulmonary plethora) | | CYANOTIC<br>RIGHT TO LEFT SHUNT | |
| | per cent | | per cent |
| *Left ventricular enlargement* | ✓ | DIMINISHED PULMONARY BLOOD FLOW | |
| ✓Patent ductus | 13 0 | NORMAL OR LOW P A PRESSURE | |
| Aorto pulmonary septal defect | 0 3 | *Left ventricular enlargement* | |
| | | Tricuspid atresia ✓ | 1 5 |
| *Right ventricular enlargement* | ✓ | Anomalous drainage of S V C or I V C into left atrium | rare |
| Atrial septal defect | 18 0 | | |
| A S D with pulmonary stenosis | 2 0 | Single ventricle with pulmonary stenosis | rare |
| Anomalous pulmonary venous drainage (partial) | | *Right ventricular enlargement* | ✓ |
| | | Fallot's tetralogy | 11 0 |
| | | Pulmonary atresia | 1 7 |
| *Enlargement of both ventricles* | ✓ | Pulmonary stenosis with reversed interatrial shunt | |
| Ventricular septal defect | 8 0 | | 3 0 |
| V S D with pulmonary stenosis | 1 3 | HIGH P A PRESSURE | |
| | | Pulmonary hypertension with reversed shunt | |
| | | i Patent ductus | 2 0 |
| | | ii Ventricular septal defect (Eisenmenger's complex) | 3 0 |
| | | iii Atrial septal defect | 1 5 |
| | | Cor triloculare biatriatum* | rare |
| | | INCREASED PULMONARY BLOOD FLOW | |
| | | Transposition of the great vessels | 1 0 |
| | | Persistent truncus | rare |
| | | Total anomalous pulmonary venous drainage into S V C or R A | rare |
| Miscellaneous 3 7 per cent | | Cor biventriculare triloculare | rare |
| Total | 4 6 | Total | 24 7 |

* Some cases may have pulmonary plethora

## DEXTROCARDIA

Mirror image dextrocardia is usually but not invariably associated with complete transposition of the viscera The heart is functionally and structurally healthy The electrocardiogram for obvious reasons shows reversal of all complexes in lead I with leads 2 and 3 interchanged (fig 8 03)

The diaphragm is always lower on the cardiac side of the chest its position not being influenced by the location of the liver or stomach

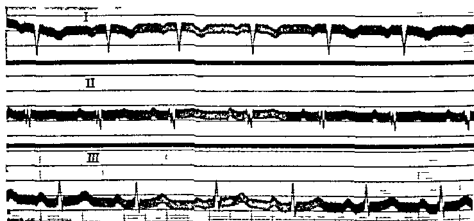



Fig 8 03—Electrocardiogram showing reversal of all complexes in lead I while lead II and III are interchanged

## IDIOPATHIC HYPERTROPHY OF THE HEART

Under this heading in the past were grouped a heterogenous collection of cardiopathies in infancy which bore little or no relationship to one another and which for the most part have since been defined in more precise terms The group included examples of von Gierke s disease anomalous left coronary artery arising from the pulmonary artery isolated myocarditis thyroid deficiency nutritional cardiopathy in infants born of diabetic mothers and fibroelastosis Nothing would be gained by discussing idiopathic hypertrophy as an entity in itself

## FAMILIAL CARDIOMEGALY

From time to time cases of cardiac enlargement are encountered in young subjects for which there is as yet no adequate explanation They are prone to paroxysmal tachycardia and atrial fibrillation and on examination there is often diastolic gallop X rays show considerable cardiac enlargement particularly of the left ventricle (fig 8 04) Left bundle branch block is usually found These patients are apt to die suddenly presumably from ventricular fibrillation or by degrees from congestive heart failure when still relatively young

Some of these cases appear to have a familial basis (Addarii *et al* 1946 Evans 1947 and 1949) Necropsy reveals myocardial fibrosis and compensatory hypertrophy of muscle Von Gierke s disease isolated myocarditis nutritional cardiopathies Friedreich s disease and abnormal coronary vessels must be excluded



Fig 8 04—Unexplained cardiac enlargement in a relatively young man (there was also left bundle branch block)

## FRIEDREICH'S ATAXIA

Cardiac manifestations associated with Friedreich's ataxia were first noted in five of six cases reported by Friedreich himself in 1863 Degeneration of muscle fibres interstitial fibrosis and compensatory hypertrophy of remaining muscle are the usual pathological findings the left ventricle being chiefly involved and the picture being not unlike that of familial cardiomegaly

In the majority there are no cardiac symptoms but the electrocardiogram may show flat or inverted T waves chiefly in antero lateral left ventricular surface leads or their equivalents or bundle branch block (Evans and Wright 1942) In a minority there are paroxysmal rhythm changes usually atrial tachycardia or fibrillation and occasionally there is fatal congestive heart failure (Russell 1946)

## CONGENITAL HEART BLOCK

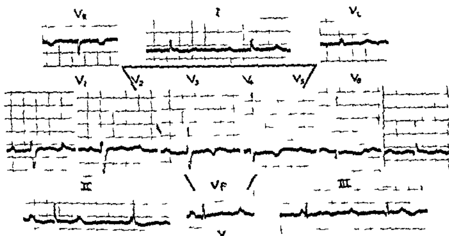
It has long been thought that congenital heart block was related to ventricular septal defect the association being accepted in 30 out of 44 cases reviewed by Yater Lyon and McNabb (1933) four of them proved at necropsy At that time however ventricular septal defect was diagnosed far too readily (Wood *et al* 1954) and there is little doubt that the

relationship has been over emphasised Thus routine electrocardiography in 200 cases of ventricular septal defect seen by Brown (1950) did not reveal heart block in a single instance In a personal series of 72 cases of isolated ventricular septal defect proved by modern methods heart block occurred only once and in 162 cases in which ventricular septal defect was associated with other anomalies it also occurred only once Conversely ventricular septal defect was not present in 13 out of a consecutive series of 15 cases of congenital complete heart block although it had been diagnosed previously in several of them

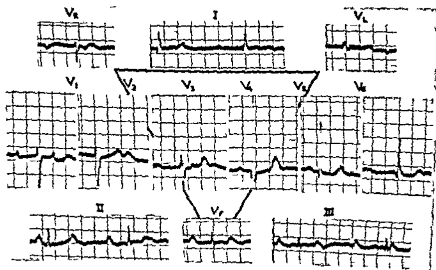
Congenital heart block is complete and permanent twice as often as it is partial or variable (Aitken 1932) Although congenital complete heart block does not differ radically from acquired heart block (q v ) it has several characteristic features of its own

1. It is present from birth and rarely may be familial (Wendkos and Study 1947)
2. The resting ventricular rate is usually faster averaging 50 beats per minute (range 36 to 80)
3. The rate commonly increases by about 33 per cent after a subcutaneous injection of atropine gr 1 75 (Aitken 1932) or on effort (Campbell and Suzman 1934)
4. In view of the faster rate and its increase on exercise effort tolerance may be almost normal and the heart but little enlarged
5. Stokes Adams fits are rare according to Brown (1950) although Janet Aitken (1932) tabulated syncopal attacks of unspecified nature in 18 per cent of the 39 cases she reviewed None of my own series of 15 cases has had a Stokes Adams seizure and only one of the eight described by Campbell and Suzman (1934) had genuine attacks It should be remembered that heart block may be acquired in cases of congenital heart disease including ventricular septal defect and Stokes Adams fits may certainly occur then as in the case reported by Rogers and Rudolph (1951)
6. A functional mitral diastolic murmur due to the large mitral stroke blood flow was heard in over three quarters of the present series particularly when the rate was under 50 and was accentuated when the atria contracted synchronously with the period of rapid ventricular filling it should not be misinterpreted as evidence of active rheumatic valvulitis
7. The QRS complex of the electrocardiogram is normal bundle branch block complexes at once suggesting an acquired lesion Inverted T waves in antero lateral chest leads over the left ventricle are not necessarily sinister in congenital heart block and may become upright on exertion (fig 8 05)

The prognosis of uncomplicated cases of congenital complete heart block is believed to be good if the ventricular rate is over 50 and still fairly




(a) At rest showing inverted T waves in chest leads




(b) After effort the rate is unchanged but the P waves are now upright

Fig. 305 —Congenital heart block with a ventricular rate of 48 beats per minute

good if the rate is between 40 and 50 The oldest in the present series was 39 and two of the others were over 30 Sudden unexpected deaths have occurred however and perhaps one should be a little guarded

Treatment when necessary is the same as for acquired cases but is rarely indicated

## VON GIERKE'S DISEASE

General enlargement of the heart sooner or later resulting in sudden death or congestive failure may be due to glycogen storage in the myocardial muscle fibres as well as in the liver, kidneys and other organs (Von Gierke 1929) Although few cases survive childhood Von Gierke's disease has been reported occasionally in adults even as late as the fifth decade It is characterised by hepatomegaly retardation of growth and sexual development persistent ketosis with acetonuria hypercholesterolæmia raised blood glycogen (normal 12-20 mg per cent) low fasting blood sugar and a flat blood sugar curve following the subcutaneous injection of 0 25 to 0 5 mg of adrenalin due to failure of mobilisation of glycogen (Ellis and Payne 1936 Crawford 1946) Some cases are familial When the heart is involved microscopy reveals heavily vacuolated muscle fibres which when specially stained are seen to be filled with glycogen It is believed that Von Gierke's disease is due to deficiency of one or more of the enzymes such as liver phosphatase that are indispensable to the breakdown of glycogen to glucose (Cori 1952)

## GARGOYLISM

Another rare congenital metabolic disorder involving the heart is gargoylism Here there is a widely distributed abnormal storage of a macromolecular glycoprotein in parenchymal fibroblastic and other connective tissue cells (Lindsay 1950) Gargoyles are mentally retarded, large headed pot bellied dwarfs with deep guttural voices deafness coarse heavy features large tongues abundant hair and other skeletal peculiarities Of 26 cases in the literature the heart was involved in 85 per cent (Emanuel 1954) There was usually interstitial myocardial fibrosis and thickening of the valves—chiefly the mitral less frequently the aortic sometimes the tricuspid and rarely the pulmonary (as in rheumatic heart disease) Many of the cases died from heart failure

## FIBROELASTOSIS

One of the relatively common causes of sudden death or rapidly fatal congestive heart failure in infancy is what is now termed fibroelastosis Affected infants may appear to be normal at birth, but within a few weeks or months suddenly develop attacks of dyspnœa and cyanosis due to acute left ventricular failure and either die suddenly in an attack or more gradually in a state of congestive failure (Adams and Katz 1952) The condition may occur alone or in conjunction with coarctation of the aorta aortic stenosis aortic atresia or mitral stenosis and is characterised by enlargement of the left ventricle overlying a uniformly thick dense white endocardium Bonham Carter (1955) has stressed its association with

hyperteleorism Good descriptions include those of Gross (1941) Prior and Wyatt (1950) and Dennis *et al* (1953)

Many of the instances of idiopathic hypertrophy of the heart reported in the older literature were undoubtedly of this nature including the critical eighth case of Kugel (1939) which was proved not to be due to glycogen storage The pathology is not yet fully understood Fœtal endocarditis was discarded by Gross (1941) A developmental defect is more probable The thickening appears to be embryonic myxomatous tissue richly supplied with elastic fibres (Glynn and Reinhold 1949) Johnson (1952) makes a good case in favour of its being due to anoxia, and describes various ways in which this might be brought about in utero including temporary closure of the foramen ovale during the development of the interatrial septum and premature closure of the foramen ovale before birth Anoxia might well be responsible for fibroelastosis in cases of anomalous left coronary artery arising from the pulmonary artery and aortic atresia with closed interventricular septum it would also explain fibroelastosis of the left atrium in cases of mitral atresia and of the right ventricle in cases of pulmonary atresia with closed interventricular septum

## ANOMALOUS CORONARY ARTERIES

A *single coronary artery* arising from the aorta may follow the normal course of the left or right coronary artery divide early into a left and right coronary artery or take an altogether atypical course with more or less equal frequency (Smith 1950) The majority of those in which the course has been normal have been found by chance in adults their average age being 45 and the oldest 80 Cardiac function is usually normal The majority of those in which the single vessel has taken an atypical course have been associated with other serious cardiac anomalies and have died in infancy

When *the left coronary artery arises from the pulmonary artery* it is set the impossible task of perfusing a high pressure chamber by means of the pulmonary artery pressure which is only about 15/7 mm Hg moreover the perfusing blood is only about 70 per cent saturated with oxygen Although the high pressure gradient between right and left coronary artery must encourage anastomotic flow this is rarely sufficient to meet the needs of the left ventricle In consequence that chamber degenerates necrosed muscle fibres may calcify surviving muscle hypertrophies the endocardium becomes fibroelastotic and the heart weight averages four times the normal (Kaunitz 1947) Clinically infants may suffer from attacks of breathlessness and peripheral cyanosis due to left ventricular failure especially when suckling angina pectoris which is not always recognised in infants may cause great distress (Bland White and Garland 1933) and sudden death is the rule The left lower lobe is not infrequently collapsed by the huge left ventricle About three quarters of all cases reported have

died in infancy usually between the third and twelfth month but a quarter have reached adult life the average age of death then being 37 years (range 17 to 64) In this small group the right coronary artery has been large and seems to have supplied both ventricles

When the *right coronary artery arises from the pulmonary artery* the situation is not the same for the right ventricle works at low pressure and is therefore much more easily perfused The left coronary artery is able to meet the demands of the base of the left ventricle posteriorly chiefly through its left circumflex branch There are usually no clinical manifestations cardiac function being normal and the anomaly is only discovered incidentally at necropsy A typical case reported by Cronk Sinclair and Rigdon (1951) died at the age of 90

## COARCTATION OF THE AORTA

The word coarctation comes from the Latin *coarctatus* meaning pressed together tightened or contracted As applied to the aorta it means a stricture of the arch usually just below the origin of the left *subclavian artery*

*Embryology* It will be recalled that on each side there are two primitive aortas each having a ventral and a dorsal part joined by an arch These three parts are called respectively the ventral aorta the dorsal aorta and the first aortic arch In front the two ventral aortas fuse to form a single tube from which develops the primitive heart the truncus arteriosus and the common ventral aorta The two dorsal aortas also fuse between the fourth thoracic and fourth lumbar segments forming a single trunk the common dorsal or descending aorta Caudal to the first pair of aortic arches spring five other pairs the six corresponding to the six branchial arches (fig 8 06a) In fishes these six vascular arches persist and supply the gills with blood for oxygenation

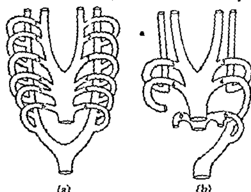


Fig 8 06 (a)—The six primitive aortic arches (b) Subsequent arrangement of the six primitive aortic arches in man (see text)

In man and mammals subsequent development is illustrated in figure 8 06b The first second and fifth arches disappear The third becomes the common carotid artery the external carotid springing from it anteriorly the internal linking up via the cranial portion of the dorsal aorta The fourth arch becomes the proximal part of the subclavian artery on the right side and the final aortic arch proximal to the junction of the ductus arteriosus on the left The sixth pair of arches is separated from the

aortic system by the aorto pulmonary septum which divides the truncus into anterior and posterior halves the anterior half becomes the ascending aorta the posterior the pulmonary artery The division of the truncus extends cranially to a point just beyond the anterior ends of the sixth pair of arches the mouths of which are included in the posterior section and therefore in the pulmonary system On the right side the sixth arch becomes the right pulmonary artery and loses its connexion with the right dorsal aorta on the left it becomes the left pulmonary artery and preserves its connexion with the left dorsal aorta in the form of the ductus arteriosus While these changes are going on harmonious alterations take place in the ventral and dorsal aortas In front the two ventral aortas fuse into a single ascending aorta as already indicated Behind the dorsal aortas undergo considerable modification the upper part forms a portion of the internal carotid artery as previously described the segment between the third and fourth arches disappears caudal to the fourth arch the dorsal aorta disappears on the right side except for that part of it which is incorporated in the right subclavian artery and forms the posterior part of the aortic arch on the left side The left subclavian artery links up with the left dorsal aorta just below the junction of the sixth arch i e just below the ductus

Many anomalies may result from faulty development of this aortic system Thus, the caudal part of the right dorsal aorta may persist so that there are two aortic arches or the caudal part of the left dorsal aorta may disappear in favour of the right so that the final aortic arch is right sided The most important however is partial obliteration of that part of the left dorsal aorta which lies between the fourth and sixth arches i e just above the ductus or between the sixth arch and the point of fusion of the two dorsal aortas i e just below the ductus This short segment of the aorta is often called the isthmus on account of the frequency with which it is narrowed but in coarctation or isthmus stenosis narrowing is extreme and often remarkably abrupt There are said to be two main types infantile and adult (Bonnet 1903) In the former (fig 8 07a) the constriction is above the ductus which remains patent and carries venous blood to the descending aorta it is incompatible with more than a few years of life In the latter (fig 8 07b) the ductus is closed or if patent the constriction is below it so that it plays no part in compensating for the defect Aortic atresia with a patent ductus

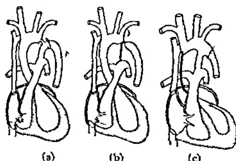



Fig 8 07—Diagrams illustrating the three main types of coarctation of the aorta
(a) Infantile type with patent ductus feeding the descending aorta
(b) Common adult type
(c) Aortic atresia with patent ductus feeding the whole systemic circulation

feeding the whole systemic circulation (fig 8 07c) constitutes a third type (Bramwell 1947) but such cases all die in infancy Other variants of these three main types have been described by Evans (1933)

This simple anatomical classification however is no longer satisfactory for it does not tally with the physiological facts and is of little practical help to the surgeon In the first place the pressure in the descending aorta is maintained by *blood flowing into the aorta from collateral channels and* by the peripheral vascular resistance not by the small quantity of blood passing through the stricture thus it is not altered by obliterating the coarctation altogether Secondly if a patent ductus joins the aorta below the stricture blood ordinarily flows from aorta to pulmonary artery as in the adult type with patent ductus for the pressure in the descending aorta is far higher than that in the pulmonary artery even when the stricture is totally occluded. In a typical case of this sort investigated by the author the pressure was 150 90 in the brachial artery 95 80 in the descending aorta and 45 27 in the pulmonary artery The catheter was passed through the ductus and emerged into the descending aorta below the coarctation The shunt was undirectional from aorta to pulmonary artery samples from the right brachial artery and descending aorta were 95 and 93 per cent *saturated with oxygen respectively the pulmonary blood flow was 12 litres* per minute or about twice the systemic flow When a patent ductus joining the aorta below the stricture actually supplies the descending aorta with venous blood it can only do so because the pulmonary vascular resistance is equal to or greater than the systemic resistance i e about eight times higher than normal This occurs in 10 to 15 per cent of all cases of patent ductus and is an essential part of the Eisenmenger syndrome (q v ) but it is not due to the coarctation Bonnet s infantile type of coarctation therefore becomes pulmonary hypertension with reversed aorto pulmonary shunt with coincidental coarctation of the aorta above the ductus It is also undesirable and unhelpful to include aortic atresia in any classification of coarctation of the aorta for it is an entirely separate entity On the other hand the site of the stricture is of the greatest importance It is proximal to the left subclavian artery in about 2 per cent of cases (Abbott 1928 Reifenstein *et al* 1947) and low usually below the diaphragm in about 2 per cent (*vide infra*)

In *presubclavian coarctation* the left arm may be under developed palpable collateral vessels and rib notching if present occur only on the right side and X rays do not show the elongated shadow of a dilated left subclavian artery above the aortic knuckle The anatomical arrangement can be seen clearly with the aid of angiocardiography or retrograde aortography via the right radial artery Such cases have so far been considered unsuitable for surgical repair

Low coarctation comprises a small group of cases in which the stricture is in the descending thoracic aorta well below the usual site or in the abdominal aorta above or below the renal arteries The group probably

includes cases of local arteritis including periarteritis and that form which has been described in young women usually under the title pulseless disease or Takayasu s disease (Caccamise and Whitman 1952) A short segment of the aorta is thickened and indurated and its lumen greatly reduced The history and subsequent course with the development of similar lesions in major peripheral arteries especially the subclavians reveal the true nature of such cases At least one of the two cases described by Bahnson *et al* (1949) seemed to be of this type and one of four abdominal coarctations in my own series is probably inflammatory (also in a young woman) But true congenital coarctation of the abrupt type can certainly occur below the diaphragm as in the 12 year old girl with hypertensive heart failure described by Kondo and his colleagues (1950) The distinguishing clinical features of low coarctation include a coarctation murmur best heard over the lumbar spine or anteriorly through the abdominal wall no palpable collateral vessels rib notching which is either absent or limited to the last two or three ribs and a normal or unfolded aortic arch radiologically Hypertension has been present in nearly all cases reported but the lesion has usually been above or has involved the renal arteries Surgical repair should be undertaken if technically feasible

A second anatomical point of practical importance is whether the coarctation is elongated or abrupt for this may determine whether or not a graft is necessary

Then if associated congenital anomalies are to be taken into account mitral stenosis fibroelastosis bicuspid aortic valve aortic incompetence and aortic stenosis each deserves as much consideration as patent ductus (*vide infra*) The commonest cause of death from coarctation in infancy for example is left ventricular failure from fibroelastosis (Bonham Carter 1955) this combination therefore has more justification to be entitled the infantile type of coarctation than Bonnet s type with a patent ductus

On the whole therefore coarctation of the aorta might be better classified quite simply according to its site nature and associated anomalies thus

CLASSIFICATION

| SITE | NATURE | ASSOCIATED ANOMALIES |
|---|---|---|
| 1 Presubclavian | Abrupt | 1 Fibroelastosis |
| 2 Isthmus | Elongated | 2 Bicuspid aortic valve (Aortic incompetence) |
| 3 Lower dorsal | Hooked | 3 Aortic stenosis |
| 4 Subphrenic | | 4 Patent ductus (with) i Direct shunt ii Reversed shunt |
| | | 5 Mitral stenosis |

*Hæmodynamics* The clinical features of the adult form of coarctation depend upon the mechanical effect of the constriction and upon the development of an extensive collateral circulation Much use is made of the branches of the subclavian artery e g the superior intercostal and the internal mammary with its intercostal superior epigastric and musculo phrenic rami also of the thoracic and subscapular branches of the axillary artery These vessels link up with the intercostal branches of the descending aorta and with the inferior epigastric branches of the femoral arteries and so by pass the constriction The blood pressure is elevated in vessels arising from the aorta above the isthmus below it the pulse pressure is much reduced systolic and diastolic pressures oscillating gently around a mean which is nearly always well below the mean brachial pressure (fig 8 08) but which may be slightly raised normal or low compared with

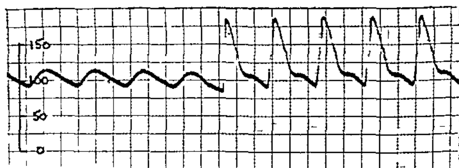



Fig 8 08—Femoral and brachial pressure pulses in a case of coarctation of the aorta

average normal controls The cause of the hypertension is uncertain A raised mean pressure in the legs does not support the mechanical hypothesis Renal ischæmia was blamed by Rytand (1938) on the grounds that hypertension was only produced experimentally when the aorta was constricted above the origin of the renal arteries according to Friedman Selzer and Rosenblum (1941) the renal blood flow is appreciably reduced in coarctation although glomerular filtration is normal In acute experiments in dogs the mean pressure in the legs is always reduced (Gupta and Wiggers 1951)

*Incidence*

Coarctation occurred in 9 per cent of a personal series of 900 cases of congenital heart disease It is said to be 4 to 5 times more frequent in men than in women (Abbott 1928 Reifenstein *et al* 1947) but the ratio was only 2 to 1 in the author s series and also in the 270 cases seen by Gross (1953) The oldest case in the literature died at the age of 92 years (quoted by Abbott 1928) Most cases seen are young adults the anomaly being discovered as a *result of mass radiography About 1 per cent of cases appear*

to be hereditary or familial although very few such instances have been published (Taylor and Pollock 1953) One of my patients for example a married woman of 34 (now 37) had a brother with coarctation who died from cerebral hæmorrhage at the age of 17 and a male cousin with coarctation who died from dissecting aneurysm or aortic rupture at the age of 37

## *CLINICAL FEATURES*

### *Symptoms*

Two thirds of clinical cases are free from all symptoms when first seen They are commonly well developed young men who have experienced no discomfort even on strenuous exercise Minor symptoms include *epistaxis* (6 per cent) *headaches* (6 per cent) or discomfort from *throbbing in the neck* *Migraine* occurs in only 2 per cent despite the frequency of mal formed cerebral vessels *Rheumatism* especially round the shoulder girdle attributed to pressure effects from dilated collateral arteries was mentioned in no less than eight of Bramwell s 26 cases but occurred in only 3 per cent of the author s series despite a routine leading question A history of rheumatic fever was obtained in 5 per cent which is the same as in controls *Intermittent claudication* in the legs occurred in 5 per cent of 212 cases combining the reports of Bramwell (1947) Christensen and Hines (1948) with my own In one instance it interfered seriously with the career of a dancer Although the measured blood flow in the legs is within normal limits at rest (Wakim Slaughter and Clagett 1948) it may not be so on effort and it usually rises after surgical treatment (Bing *et al* 1948) The blood flow in the arms is usually elevated at rest and falls post operatively

Major symptoms are always due to complications and will be discussed later

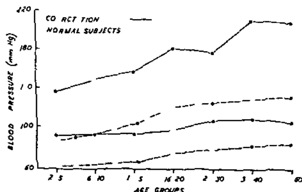



Fig 8 09—Chart showing the relationsh p between blood pressure and age in cases of coarctation of the aorta compared with normal controls

*Physical signs*

(1) *Excessive pulsation of the carotid arteries* may be visible on inspection

(2) *The blood pressure in the arms* is raised moderately and both systolic and diastolic levels rise gradually with the years much as they do in normal subjects (fig 8 09) There is no vicious circle mechanism because the renal vessels are protected The blood pressure rises sharply on exercise at least during the first few minutes but probably no more than in patients with essential hypertension of similar degree Diminished pulsation in the left subclavian artery may be due to presubclavian coarctation an anomalous vessel or compression from an aortic aneurysm Diminished pulsation in the right subclavian is nearly always due to its having an anomalous origin

(3) The blood pressure in the legs is lower than in the arms in all but the mildest cases Femoral pulsation is poor and at times impalpable (20 per cent) The small pulse is obviously delayed in 95 per cent of cases in which it can be felt Direct arterial tracings reveal a wave form that looks grossly overdamped or not unlike the pattern of a mean arterial pressure (fig 8 08)

In 21 cases investigated by Brown *et al* (1948) at the Mayo Clinic the pressure in the radial artery averaged 196/96, and in the femoral 113/81, whereas in controls they were identical the onset of the femoral pulse was delayed by an average of 0 03 second and the peak by 0 08 second The mean pressure in the femoral artery is usually within normal limits or may be a little low, but it is rarely raised If the femoral arteries were palpated as a routine very few cases of coarctation would be overlooked



Fig 8 10—A visible collateral anastomotic intercostal artery in a case of coarctation of the aorta

(4) *Visible or palpable pulsation of collateral vessels* particularly in the interscapular region posteriorly (fig 8 10) can be demonstrated in about 80 per cent of cases in the age groups usually seen (Christensen and Hines 1949) but is unusual in small children Tortuous and dilated intercostal vessels show up better if the patient bends forward with the arms hanging down—Suzman's sign (Campbell and Suzman 1947)

The *retinal arteries* may be normal tortuous or somewhat constricted but serious hypertensive retinopathy does not occur

Retinal hæmorrhages are seen occasionally however and subhyaloid hæmorrhage may accompany a subarachnoid bleed Papillœdema at once points to a different etiology as was substantiated in two of my cases

*The heart* itself has all the usual features associated with moderate hypertension (q v ) It is hypertrophied rather than dilated and rarely fails in the absence of complications at least under the age of 50 (Reifenstein *et al* 1947) The cardiac output in uncomplicated cases is normal (Bing *et al* 1948) Left ventricular failure in infancy is commonly due to associated fibroelastosis, and *in older children or relatively young adults* to aortic stenosis or incompetence, mitral valve disease other congenital anomalies such as ventricular septal defect and patent ductus or bacterial endocarditis (*vide infra*)

*Auscultation*

In uncomplicated cases an *aortic systolic murmur* often initiated by an ejection click is usually heard at the apex and base

In practically one third of my cases a *mitral diastolic murmur* was heard at the apex indistinguishable in timing pitch intensity and duration from the Carey Coombs murmur of active rheumatic carditis (Wood 1950) In arriving at this figure of 33 per cent three cases of rheumatic mitral stenosis and five cases in which turbulence could have been due to an excessive mitral blood flow (three with patent ductus and two with ventricular septal defect) were excluded It is inconceivable that a murmur heard so frequently could have been due to active rheumatic valvulitis although this was believed to be the explanation in one instance the erythrocyte sedimentation rate was practically never raised subacute rheumatism rheumatic fever or chorea past or present was no more frequent than in controls (5 per cent) and the incidence of rheumatic mitral stenosis in adults with coarctation was only 2 per cent A similar murmur may be heard in congenital aortic stenosis and in both conditions slight thickening of the mitral cusps due to minor fibroelastotic changes provide a possible though purely speculative explanation The murmur may or may not disappear after successful surgical treatment

The third important murmur of uncomplicated coarctation is heard posteriorly between the scapulæ and is due to the jet produced by the stricture It may spill into diastole as demonstrated phonocardiographically by Wells Rappaport and Sprague (1949) It was heard high up in the typical situation in 85 per cent of the present series and in four cases in which aortic stricture was proved to be subphrenic (only one of them thought to be congenital) the murmur was only heard posteriorly in the lumbar region and anteriorly through the abdominal wall There is therefore strong evidence that the site of the posterior murmur at once distinguishes classical coarctation from the subphrenic variety According to both Abbott (1928) and Reifenstein *et al* (1947) there is complete occlusion of the aorta at the site of coarctation in about one quarter of all cases

come to necropsy It is not unlikely therefore that the 15 per cent of my series that did not have the murmur had complete occlusion It is admitted that large collateral vessels may sometimes cause a murmur, for digital compression of such a vessel may abolish it but this is exceptional and as a rule the murmur cannot be influenced by digital compression of any of the palpable collateral arteries That a coarctation jet may cause a murmur (and thrill) has been verified at operation

*Electrocardiogram*

In the present series the electrocardiogram was strictly normal in 46 per cent and showed slight left ventricular preponderance, as judged by the voltage of QRS in 23 per cent Marked left ventricular preponderance with inverted T waves in leads $V_5$ and $V_6$ occurred in 20 per cent and three quarters of these cases had well developed aortic valve disease usually stenosis Thus in uncomplicated coarctation only 5 per cent of cases showed electrocardiographic evidence of serious left ventricular strain

Right bundle branch block occurred in 11 per cent only a quarter of this small group had a patent ductus the other cases being straightforward Ziegler (1954) suggested that right bundle branch block might represent a residual change from strong right ventricular preponderance in utero when the fœtal ductus joined the aorta above the stricture

*X ray appearances*

There are three virtually diagnostic X ray signs of coarctation of the aorta elongation of the aortic knuckle due to dilatation of the left subclavian artery (64 per cent) post stenotic dilatation of a short segment of the descending aorta which can be seen clearly in the postero anterior view (61 per cent) and notching of the inferior margin of the ribs (51 per cent) The figures given are from my own series

*Dilatation of the left subclavian artery* also obliterates the supraaortic triangle in the second oblique position (Evans 1952) Even when not distinguished clearly in the anterior view it seems to change the outline of the aortic knob so that the latter rarely looks normal

*Post stenotic dilatation* of the proximal end of the descending aorta immediately below the stricture was described by Bramwell (1947) as a double aortic knuckle (fig 8 11) It is a most important sign for it shows the presence and site of the stricture itself

*Notching of the inferior margins of the ribs* (fig 8 12) known as Dock's sign, is due to pressure erosion from dilated intercostal arteries (Railsbach and Dock 1929 Dock 1948) In my series it was seen in only one fifth of children under 12 years of age the youngest with notching was six Its higher incidence in past literature (about 80 per cent) may be due to the fact that coarctation was frequently overlooked in children and that notching of the ribs *per se* was perhaps the chief means of detecting it

*Enlargement of the left ventricle* was relatively slight or radiologically absent in 85 per cent of the cases Considerable enlargement was present

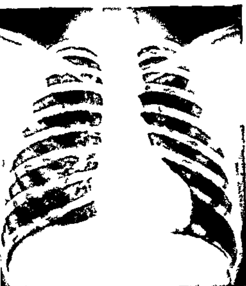


Fig 8 11—Post stenotic dilatation of the top of the dorsal aorta in a case of coarctation

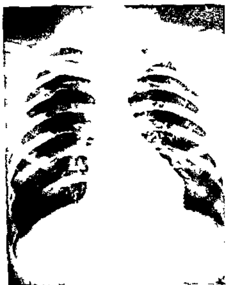


Fig 8 12—Rib notching (Dock's sign) in coarctation of the aorta



Fig 8 13—Mild coarctation of the aorta demonstrated by means of angiocardiography there is post stenotic dilatation of the proximal segment of the dorsal aorta and overlapping of proximal and distal segments owing to the plane in which the picture has been taken



Fig 8 14—The abrupt type of coarctation of the aorta demonstrated by selective angiocardiography diagnol having been injected directly into the pulmonary artery through a wide bore catheter

in 15 per cent but nearly all of these cases had serious aortic valve disease or were otherwise complicated

*Entirely normal X ray appearances* were seen in only 5 per cent of cases Aortic aneurysm usually mycotic and very close to the stricture was seen in two instances

The constriction itself (figs 8 13–8 16) may be demonstrated clearly by means of angiocardiography (Grishman Steinberg and Sussman 1941) or retrograde aortography (Broden Hanson and Karnell 1948)



Fig 8 15—Angiocardiogram demonstrating the hooked type of coarctation



Fig 8 16—Angiocardiogram in a case of coarctation of the aorta with complete occlusion showing marked dilatation and tortuosity of collateral channels

## ASSOCIATED ANOMALIES

*Bicuspid aortic valve* occurred in 23 5 per cent of 200 autopsied cases reviewed by Abbott (1928) and in 42 3 per cent of 104 autopsied cases reviewed by Reifenstein Levine and Gross (1947) It is the usual cause of the aortic diastolic murmur that has been heard so frequently—in 20 per cent of 96 cases reported by Christensen and Hines (1948) and in 10 per cent of the author s series It was recorded phonocardiographically by Wills Rappaport and Sprague (1949) in 5 out of 15 cases of coarctation Aortic incompetence is rarely severe however unless bacterial endocarditis supervenes

*Significant aortic stenosis* presumably congenital occurred in 7 5 per cent of the author s series and calcific aortic stenosis was reported at necropsy in 11 per cent of the fatal cases collected from the literature by Reifenstein *et al* (1947) The presence of calcium however does not invalidate a congenital etiology (Campbell and Kauntze 1953) The stenosed valve is usually bicuspid (Smith and Matthews 1955) It is by no means easy to be sure whether aortic stenosis is present or not in cases of coarctation with

a basal systolic thrill and large left ventricle A convincing anacrotic pulse is exceptional the blood pressure is still raised and the aortic second sound may be loud An aortic systolic thrill without any other evidence of stenosis was appreciated in only three per cent of the series Two other cases thought to have some degree of aortic stenosis on account of considerable left ventricular enlargement and strong left ventricular preponderance electrocardiographically in addition to the thrill did not have a pressure gradient across the aortic valve at operation although in one of them the central aortic tracing looked stenotic in form Although the significance of a systolic thrill over the root of the aorta in cases of coarctation must remain in doubt the fact remains that judged on other grounds particularly on the size of the left ventricle and electrocardiographic evidence of left ventricular strain 75 to 85 per cent of such cases have aortic stenosis

The lesion is important because it increases the risk of surgical repair and because such repair may be valueless unless aortic valvotomy is also undertaken

*Patent ductus arteriosus* with most of the usual clinical features occurred in 7 per cent of my series The shunt was always from left to right whether the ductus joined the aorta above or below the stricture Rib erosion and a demonstrable collateral circulation were evident in only one instance their absence in the presence of patent ductus being noted by Bramwell (1947) in his three cases

Four remarkably illustrative cases were published by Edwards *et al* (1949) judged by the clinical features the microscopical appearances of the small pulmonary vessels and the relative sizes of the two ventricles at necropsy there was pulmonary hypertension with reversed shunt in two of them and a direct aorto pulmonary shunt in the other two the ductus joined the aorta above the coarctation in one of those with reversed shunt and in one with direct shunt and it joined below the coarctation in one each of these two functionally different types also

Patent ductus presents no special problem when complicating coarctation of the aorta in children or adults It should be ligated or divided at the same time as the stricture is repaired provided the shunt is from aorta to pulmonary artery if the shunt is reversed both the ductus and the coarctation should be left alone

*Ventricular septal defect* complicating coarctation of the aorta occurred in 2 per cent of this series and presents a rather similar physiological picture the raised pressure in the left ventricle tending to increase the left to right shunt

In a case investigated by the author and subsequently proved at necropsy the mean pulmonary arterial pressure was 95 mm. Hg whilst that in the right ventricle was 55 mm. Hg Samples from the pulmonary artery were 86 per cent saturated with oxygen from the middle of the right ventricle 70 per cent and from the right atrium and superior vena cava 60 per cent Clinically coarctation of the aorta was recognised by the presence of high blood pressure in the carotid




Fig 8 17—Coarctation of the aorta associated with patent interventricular septum proved at necropsy

and subclavian arteries (160 100 mm Hg in a boy of six) with an immeasurable pressure in the legs but there was little evidence of a collateral circulation The pulmonary arteries were grossly engorged radiologically (fig 8 17) there was a pulmonary diastolic murmur at the base and a mitral diastolic murmur with triple rhythm at the apex Despite the absence of a machinery murmur patent ductus arteriosus was believed to be responsible for the shunt and seemed to be confirmed by the catheter findings the raised oxygen content of the right ventricular sample being attributed to pulmonary incompetence At necropsy coarctation of the aorta of the adult type was associated with a large defect of the membranous interventricular septum The aortic cusps were normal the aortic ring admitted only the little finger and the ascending aorta was small The defect in the septum admitted the middle finger whilst the pulmonary ring admitted both middle and fore fingers A very small patent ductus joined the aorta below the isthmus Although the huge pulmonary artery did not sit astride the septal defect there could be no doubt that the major portion of the left ventricular contents was expelled into that vessel The mitral diastolic murmur was clearly functional for there was no sign of mitral stenosis Both ventricles were greatly enlarged the left retaining its natural dominance

*Fibroelastosis* (q v ) appears to be the chief cause of heart failure and death in infants with coarctation of the aorta and usually makes surgical repair at that age pointless (Bonham Carter 1955) *It seems to be rare in* the large number of cases that survive infancy Whether a minor degree of fibroelastosis is responsible for an unusual degree of left ventricular

enlargement in children or for any of the aortic or mitral anomalie sometimes associated with coarctation is unknown

*Variations in one or other subclavian artery* rarely both occur in about 5 per cent of cases (King 1937) and may be due to its anomalous or stenotic origin (East 1932 Love and Holms 1939) Presubclavian coarctation is a rare cause of a small pulse in the left arm

## COMPLICATIONS

Since practically all the important complications of coarctation of the aorta used to be fatal their relative frequencies are known from previous necropsy studies The figures from two carefully documented series in the literature those by Abbott (1928) and by Reifenstein Levine and Gross (1947) are tabulated below

FREQUENCY OF COMPLICATIONS

| CAUSE OF DEATH | ABBOTT (per cent) | REIFENSTEIN *et al* (per cent) | AVERAGE AGE (years) |
|---|---|---|---|
| Aortic rupture (or dissection) | 20 | 23 | 25 |
| Bacterial endocarditis (or endarteritis) | 16 | 2 | 2) |
| Cerebral vascular accident | 12 5 | 11 | 28 |
| Congestive heart failure | 29 | 18 | 39 |
| Incidental | 22 5 | 26 | 47 |

*Aortic rupture* is through the ascending aorta in 80 per cent of the cases and just distal to the coarctation in the remainder The ascending aorta is thin walled and rupture usually means dissection into the pericardium (Reifenstein *et al* 1947)

*Bacterial endocarditis* infecting a bicuspid aortic valve is three times more common than bacterial endarteritis involving the aorta immediately adjacent to the coarctation usually just below it (Reifenstein *et al* 1947)

*Saccular aneurysm* of the descending aorta in the immediate neighbourhood of the stricture usually just below it is seen in about 3 per cent of cases (Abbott 1928 Gross 1953) and is nearly always secondary to bacterial endarteritis There were two instances in the present series of 90 cases both of which were due to previous bacterial endarteritis Calcification in the wall of the aneurysm is the rule and occurred in each of the two mentioned One of them had the coarctation and the aneurysm excised and successfully replaced with a graft by Sir Russell Brock

*Cerebral vascular accidents* usually subarachnoid hemorrhage may be due to rupture of a berry aneurysm or of a vessel weakened by defective or

degenerative elastic tissue (Glynn 1940) Similar defects may be found in other vessels including the aorta (Davies and Fisher 1943) Hypertension presumably encourages the disaster

*Heart failure* is rare in uncomplicated cases under 40 years of age but takes an increasing toll as age advances even then some new complication may be responsible as in two of three cases that were observed over a period of 25 to 30 years when the development of heart block precipitated the breakdown (Newman 1948) As previously stated heart failure in infancy is usually due to associated fibroelastosis and in children or relatively young adults to aortic stenosis or incompetence bacterial endo carditis other congenital anomalies such as patent ductus and ventricular septal defect or coincidental rheumatic heart disease

*Mitral valve disease* may complicate coarctation of the aorta but probably not more often than would be expected from its known frequency of 2 per cent in the general population Unquestionable rheumatic mitral stenosis occurred in only two of the series reported here and in one of them Sir Russell Brock undertook mitral valvotomy at the same time as he successfully repaired the coarctation Relatively mild organic mitral in competence may be aggravated by the hypertension associated with coarctation but this was only witnessed in one instance Amongst the children there was only one convincing case of rheumatic valvulitis in which a soft mitral diastolic murmur was heard for the first time after an attack of rheumatic fever Congenital mitral stenosis was not observed in this particular series but is a real although rare association

*Pregnancy* in cases of coarctation deserves a note The raised blood pressure may be discovered for the first time in an ante natal clinic and this is one of the standard ways in which the presence of coarctation comes to be recognised Of 96 instances collected from the literature by Rosenthal (1955) including 5 of his own 11 died during pregnancy chiefly from aortic rupture just before or during labour

## *PROGNOSIS AND TREATMENT*

Although many patients live well into middle life without serious handi cap some even to the eighth decade the majority succumb between the ages of 20 and 40 to one of the complications mentioned above (Abbott 1928) The average age of death is 35 (Reifenstein Levine and Gross 1947) Surgical repair (Crafoord and Nylin 1945 Crafoord 1948) should therefore be offered The physiological results of such an operation are usually good the blood pressure falls symptoms disappear the heart becomes smaller and it may be assumed that the risks of intracranial hæmorrhage aortic rupture and late heart failure are diminished Bacterial endocarditis on bicuspid aortic valves should not be prevented

The constriction is excised and the two ends joined together by direct suture or by means of an aortic homograft (Gross 1951) A patent ductus

may be ligated or a post stenotic mycotic aneurysm removed at the same time The mortality rate attending the resection has fallen from 16 per cent in 1949 (Shapiro) to under 5 per cent A series of papers by Gross (1949 1950 1953) illustrates this very well by 1953 he had operated on 270 cases in the first hundred of these (reported in 1950) there were eleven deaths in the last hundred only two Over the last five years our total surgical mortality rate at the Brompton hospital has been 8 per cent According to Gross (1953) the optimum time for the operation is between the ages of 10 and 20 years but 11 per cent of his cases were between 30 and 40 years old and the blood pressure may fall to normal even at this age Grafts become endothelialised but remain inert They seem capable of withstanding the blood pressure indefinitely

*Selection of cases for surgery*

Now that the operative mortality rate is under 5 per cent it is probably right to advise all patients with uncomplicated coarctation of the aorta to have it repaired between the ages of 7 and 30, the earlier the better An exception should be made if the stricture is trivial judged by a normal or near normal blood pressure good femoral pulsation without clinically detectable delay and no collateral circulation clinically or radiologically The diagnosis in these rare cases is made on the presence of a coarctation murmur posteriorly and post stenotic dilatation of the aorta radiologically it may be confirmed by means of angiocardiography

The effect of complications on the question of surgical treatment has already been discussed

## RIGHT SIDED AORTA

As an isolated anomaly a right sided aortic arch joining a right dorsal aorta is rare and is discovered radiologically by chance (fig 4 31) Its radiological features (Bedford and Parkinson 1936) have already been described in Chapter IV Clinically it is of no significance

It may be important however when associated with other congenital anomalies because its presence may help their identification For example a right sided aorta occurs in some 20 per cent of cases of Fallot s tatralogy but not in pulmonary stenosis with normal aortic root again it may occur in Eisenmenger s complex proper but not in pulmonary hypertension with reversed shunt through a patent ductus or atrial septal defect

## AORTIC RINGS

During the development of the aortic system certain anomalies may arise which may compress the œsophagus or trachea and cause dysphagia or distressing attacks of wheezing and choking in infancy Broncho pneumonia is a common complication and not infrequently fatal If the infant survives symptoms usually disappear as the vessels lengthen (Apley,

1949) but may return again with middle age owing to the development of arteriosclerosis (Sprague *et al* 1933) The chief anomalies responsible for this clinical syndrome are double aortic arch aberrant right subclavian artery and a ligamentum arteriosum joining a right aortic arch to the left pulmonary artery (Gross and Neuhauser 1951) The vascular arrangements are varied (Edwards 1948) but the three most common varieties may be described here

In *double aortic arch* the primitive fourth right arch which normally involutes distal to the innominate artery persists and joins the primitive *left* dorsal aorta Beyond the origins of the right subclavian and right common carotid arteries anteriorly the anomalous vessel courses posteriorly behind the trachea and œsophagus and links up with the normal anterior arch below the origin of the left subclavian artery where they join to become a left dorsal aorta The effect is to encircle the trachea and œsophagus

A *right sided aortic arch crossing behind the œsophagus* to join a left dorsal aorta may constrict the œsophagus and trachea by being pulled forward by a patent ductus or ligamentum arteriosum connecting it to the left pulmonary artery (Neuhauser 1949) It should be understood that an ordinary right sided aortic arch joins the *right* dorsal aorta the left dorsal root involuting so that the completed aorta courses down the right side of the thorax and causes no trouble

An *aberrant right subclavian artery* arises from the aorta distal to the left subclavian artery and passes across to the right and upwards behind the œsophagus, which it indents obliquely The filling defect of the barium filled œsophagus can be seen radiologically (Brean and Neuhauser 1947) *Lifelong dysphagia has been caused by this anomaly (Bayford 1789)*

All three anomalies may be modified surgically in such a way as to relieve the pressure on the trachea and œsophagus In double aortic arch the anterior channel can be divided between the left common carotid and left subclavian arteries a patent ductus or ligamentum arteriosum completing a vascular ring can be divided and an aberrant subclavian artery can be divided collateral pathways ensuring an adequate blood supply to the limb (Gross and Neuhauser 1951)

The whole rather complicated subject has been well reviewed by Brown (1950)

## AORTIC HYPOPLASIA

Hypoplasia of the aorta is a common manifestation of Marfan's syndrome (q v) as pointed out by Baer Taussig and Oppenheimer (1942) Only the ascending aorta is usually involved especially at its root within the pericardium Pathologically it presents initially with features indistinguishable from cystic medial necrosis and later with degeneration and disruption of the elastic lamellæ disorganised masses of hypertrophic and hyperplasic smooth muscle, and numerous dilated vascular channels

penetrating the media from the adventitia (McKusick 1955) At first it is clinically unrecognisable unless the ascending aorta looks peculiarly small Sooner or later however dilatation of the aortic ring may lead to free aortic incompetence, the ascending aorta may become obviously dilated or the aorta may rupture or dissect without warning usually into the pericardial sac

Coarctation of the aorta is rarely associated with arachnodactyly but the pathological appearances of the ascending aorta in cases of aortic rupture or dissection secondary to coarctation are similar to those described above

Occasionally hypoplasia of the aorta is seen without any such associations and in rare instances hypoplasia and dilatation of the pulmonary artery accompany it (fig 8 18) The case illustrated was in a man of 33 with no symptoms and no abnormal physical signs cardiac catheterisation also revealed nothing abnormal

In these days of mass radiography difficulty may be experienced in trying to interpret the significance of an unusually prominent aorta as an isolated finding in a young individual The attitude advised is to take a serious view of any such anomaly if there is any trace of Marfan's syndrome in the family or if the apparent dilatation ceases abruptly at the origin of the innominate artery If neither condition applies the peculiarity may be better disregarded for the time being and treated as a normal variation

## CONGENITAL AORTIC INCOMPETENCE

Aortic incompetence may be due to a bicuspid or quadricuspid aortic valve (*vide infra*) especially under the stress of hypertension whether acquired or due to associated coarctation of the aorta anomalous aortic valve cusps however may leak without any complication sometimes quite freely

The second important cause of congenital aortic incompetence is dilatation of the root of the ascending aorta as seen characteristically in Marfan's syndrome (q v ) The leak in these cases is usually considerable and may be already well advanced at a time when the radiologically visible part of the ascending aorta still looks normal The prognosis in such cases is poor the risks being aortic rupture or dissection and heart failure

A third and rare cause of congenital aortic incompetence is ventricular septal defect (q v )

## BICUSPID AORTIC VALVE

Abbott (1932) estimated the incidence of bicuspid aortic valve at 1 3 to 1 4 per cent Owing to the frequency of superimposed infection or sclerosis it is often difficult to be sure microscopically whether a disorganised valve is congenitally bicuspid or not but Lewis and Grant (1923) put its scopic recognition on a firm basis

1949) but may return again with middle age owing to the development of arteriosclerosis (Sprague *et al* 1933) The chief anomalies responsible for this clinical syndrome are double aortic arch aberrant right subclavian artery, and a ligamentum arteriosum joining a right aortic arch to the left pulmonary artery (Gross and Neuhauser 1951) The vascular arrangements are varied (Edwards 1948) but the three most common varieties may be described here

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## AORTIC HYPOPLASIA

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At the time of Abbott's review 46 per cent of 147 proved cases and 21 per cent of 316 proved or probable cases of bicuspid aortic valve had coarctation of the aorta Conversely she calculated that 28 5 per cent of cases of coarctation had a bicuspid aortic valve Its significance in this condition has already been described

Apart from its association with coarctation bicuspid aortic valve is clinically important for three main reasons (1) it may leak spontaneously or as a result of acquired hypertension an insidious sclerosing process increasing this tendency (2) about one quarter of all cases become infected sooner or later (3) an associated weakness of the sinuses of Valsalva may lead to aneurysmal dilatation or rupture

## AORTIC ATRESIA

Clinically this is unimportant since it is rarely compatible with more than a few days of life (Roberts 1936) it is also very uncommon (Brown 1950) Pulmonary hypertension with reversed shunt through a patent ductus allows venous blood to be transported to the systemic circulation Oxygenated blood can only escape from the lungs via broncho pulmonary anastomotic venous channels unless there is an atrial septal defect or anomalous pulmonary venous drainage Even with a large atrial septal defect the situation is wholly unsatisfactory for if a proper systemic output is to be maintained the pulmonary vascular resistance must be very high and this must prevent an adequate pulmonary blood flow According to Horley (1955) all reported cases have had fibroelastosis of the left ventricle unless the interventricular septum has been patent He suggests that both the complete fusion of the aortic cusps and the fibroelastosis may be due to anoxia resulting from the temporary formation of a complete im penetrable interatrial septum during some period of its development

## AORTIC STENOSIS

*Pathology*

Congenital aortic stenosis may be valvular due to fusion of the cusps or subvalvular due to defective absorption of the primitive bulbus cordis, in the latter type a perforated membrane lies proximal to the valve (Keith 1924) Although in Abbott's necropsy series of 1 000 cases of congenital heart disease aortic valve stenosis was present in 11 and subaortic stenosis in 12 (Abbott 1931 and 1951) it is now generally believed that the great majority of cases are valvular All degrees of severity are encountered and it is probable that some of the relatively mild cases end up with calcific stenosis when they may be mistaken for rheumatic strictures (Campbell and Kauntz 1953) Even at necropsy it may be very difficult if not impos sible to make certain of the etiology when infective or sclerosing processes have grossly distorted the whole structure of the valve It is not possible clinically to distinguish the two types of congenital aortic stenosis

*Incidence*

Aortic stenosis accounted for 3 per cent of the 900 cases of congenital heart disease in this series There were three males to one female as in Campbell s series A congenital etiology was accepted if a loud aortic systolic murmur was first heard in infancy if any other congenital anomaly was present if there was a strongly suggestive family history such as that described by Davies (1952) or if an obviously tight stricture was found in childhood in the absence of a history of rheumatism or chorea

*Clinical features*

Although the clinical features of congenital aortic stenosis are more or less similar to those of acquired rheumatic stenosis (q v ) there are minor points of difference that deserve emphasis

Of the 30 patients in the author s series only five of whom were over 18 years old symptoms were absent in 18 slight in two and moderate in five None had frank left ventricular failure Only one had angina pectoris and only two had syncopal attacks on effort For the most part therefore aortic stenosis is well tolerated in those that survive infancy infant mortality however is high the average age of death in Abbott s series for example being 3 75 years and this must account for the rarity of severe cases in later childhood and adolescence

Of the well known physical signs of aortic stenosis (q v ) the peripheral pulse was normal in 15 small but not otherwise characteristic in 12 and detectably anacrotic in only three The left ventricle was a little heaving clinically in two thirds (but rarely displaced much to the left) normal or a little bulky radiologically (but not dilated) in 86 per cent and hypertrophied electrocardiographically in two thirds (considerably so with inverted T waves in leads $V_5$ and $V_6$ in a quarter) A loud aortic systolic ejection murmur usually heard as well at the apex as at the base and always accompanied by a well marked thrill was heard in all and since our attention was drawn to it by Leatham (1954) an aortic ejection click has also been heard in all but one instance The second heart sound was split normally in half the cases A falling before P it was clinically single in a third however due to delay in the aortic component and the split was reversed in two instances When single the second sound could usually be well heard over the carotid and over the left ventricle at the apex beat as well as at the base from which the presence of the aortic element was inferred An aortic diastolic murmur was heard in only 10 per cent which contrasts rather strongly with the 45 per cent incidence of associated aortic incompetence in the series reported by Campbell and Kauntz (1953) but this may be a matter of selection for we were at first disinclined to accept a diagnosis of congenital aortic stenosis in the presence of obvious incompetence A soft mitral diastolic murmur indistinguishable from that heard in many cases of coarctation of the aorta was detected in one sixth of this small series

The electrocardiogram provided the best evidence of the degree of left ventricular hypertrophy and has already been referred to

The X ray appearances were very similar to those described by Campbell and Kauntz (1953) The ascending aorta is usually a little prominent and curved out to the right but the aortic knuckle is normal or inconspicuous The left ventricle looks dense and hypertrophied rather than dilated so that the cardiothoracic ratio is not much increased

Cardiac catheterisation in six relatively mild cases revealed normal pulmonary artery pressures normal arteriovenous oxygen differences (average 32 ml per litre) and of course normal cardiac outputs

*Prognosis*

Severe cases usually die in infancy The majority of those seen in childhood are mild or relatively so and have a good prognosis Precise figures are difficult to arrive at in view of uncertainty concerning etiology in old calcific cases of aortic stenosis A minority in which the stenosis is more severe may die suddenly when young especially those with a history of angina pectoris or syncope on effort (Marquis and Logan 1955)

*TREATMENT*

Aortic valvotomy should be advised when serious symptoms begin to develop in severe cases

## MITRAL STENOSIS

Congenital mitral stenosis is exceptionally rare being found in only six of Abbott s 1 000 cases Three examples are included in my own series of 900 clinical cases, one of them confirmed at operation Out of 43 collected from the literature by Ferencz Johnson and Wiglesworth in 1948 (to which they themselves contributed nine) only eight were isolated by far the most common association was fibroelastosis (25) next came patent ductus (17) then aortic valvular stenosis (12) coarctation of the aorta (7) and ventricular septal defect (2) The great majority died in infancy

The clinical features appear to be similar to those of rheumatic mitral stenosis but are usually modified by the associated lesion In those who survive infancy the commonest associated lesions are patent ductus and coarctation of the aorta

Mitral valvotomy is advised if the symptoms warrant it although it may be awkward technically owing to difficulty in recognising exactly where the commissures should be D Abreu undertook the operation in two cases one of which had a patent ductus (Bower *et al* 1953) and Sir Russell Brock operated on one for me ligating a patent ductus at the same time

The increased pulmonary blood flow from the patent ductus might be expected to cause death from pulmonary œdema at an early age in these cases but in the patient mentioned a girl of 19 the pulmonary vascular resistance was high and cyanosis from shunt reversal began when she was only 18 months old and may

well have saved her life Cyanosis on effort increased a little over the years and was sufficiently differential to cause no clubbing of the fingers but at least moderate clubbing of the toes the hæmoglobin was 104 per cent there was of course no Gibson murmur the physical signs being those of mitral stenosis with moderate pulmonary hypertension and X rays showing a combination of pulmonary venous congestion and slight plethora Cardiac catheterisation (when she was 17 years old) revealed an indirect left atrial pressure of 18 mm Hg above the sternal angle a pulmonary artery pressure of 96/58 (rising to 130/90 on effort) a simultaneous right brachial pressure of 120/60 and bidirectional shunt the pulmonary artery sample being 74 per cent saturated the right ventricular sample 65 per cent and the right brachial 87 per cent Unfortunately no femoral sample could be obtained at the time but from our experience of reversed shunts in patent ductus (confirmed by means of angiocardiography in this case) the femoral sample could hardly have been above 80 per cent saturated The pulmonary blood flow worked out at 6 litres per minute and the pulmonary vascular resistance at 10 units It was argued that although shunt reversal was taking place the pulmonary blood flow was still above normal the pulmonary resistance was only borderline between high and extreme and that if the left atrial pressure were lowered the left to right shunt would increase It was decided therefore to advise ligating the duct as well as mitral valvotomy At operation the mitral orifice measured 1 25 × 0 75 cm and the duct 1 5 cm long and 1 5 cm wide both much as predicted

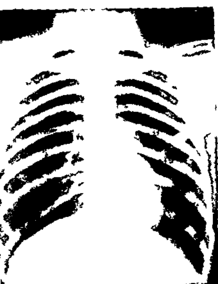
A year later she was looking and feeling well there was no cyanosis and no evidence of right ventricular embarrassment while her effort tolerance had increased considerably There were still well marked signs of mitral stenosis however for a complete valvotomy had not been achieved owing to the technical difficulty mentioned earlier

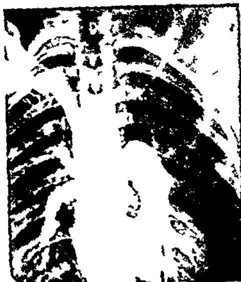
## COR TRIATRIATUM

A physiological situation very similar to that produced by congenital mitral stenosis may be caused by the anomalous development of a transverse septum which separates that part of the left atrium joined by the pulmonary veins from the rest of the chamber In the case reported by Barnes and Finlay (1952) the anomalous septum was perforated by a small hole measuring only 2 mm in diameter through which the whole cardiac output had to pass There was intense pulmonary venous congestion but no evidence of mitral stenosis Pedersen and Therkelsen (1954) described a similar case in which cardiac catheterisation revealed typical evidence of mitral stenosis at operation the mitral valve was normal and the anomalous septum was overlooked

## IDIOPATHIC DILATATION OF THE PULMONARY ARTERY

Mass radiography brings an increasing number of cases for cardiological review on account of real or apparent dilatation of the pulmonary artery as an isolated abnormality Quite a number of such cases can be dismissed





(a) Anterior view (b) Angiocardiogram

Fig 8 19—Apparent dilatation of the pulmonary artery in a normal subject

immediately as variants of normal or as rotational effects (fig 8 19) In the example illustrated the left pulmonary artery is responsible for the left middle arc and the angiocardiogram prove that the pulmonary artery is not dilated (cf fig 8 16c) There remain however a small group of cases in which the pulmonary artery is undoubtedly dilated for no apparent reason (Laubry Routier and de Balsac 1941)

There are no symptoms and no abnormal physical signs in uncomplicated cases except a pulmonary ejection click which is common and a soft pulmonary systolic murmur which is perhaps less common The second heart sound is physiologically split and the pulmonary component of average intensity The electrocardiogram is normal Angiocardiography is the only reliable way of proving the existence of true dilatation (fig 8 16c)

Cardiac catheterisation whilst demonstrating essentially normal pressures and flows not infrequently reveals a slight systolic pressure gradient of 5 to 10 mm Hg across the pulmonary valve the right ventricular pressure however is not above normal The significance of this phenomenon which was recorded consistently in four out of eight such cases catheterised and which was noted by Cournand Baldwin and Himmelstein (1949) is not yet understood Trivial pulmonary valve stenosis is difficult to exclude and in some of the cases the tracings themselves are unsatisfactory and suggest an artefactual gradient

Functional pulmonary incompetence may complicate cases of idiopathic dilatation and despite the normal pressure in the pulmonary artery may be considerable in degree Conspicuous dilatation of the right ventri

results and the electrocardiogram may show prolonged right ventricular activation Secondary tricuspid incompetence and final overloading of the right ventricle may complete the breakdown Admittedly such cases are rare but they may serve to correct an impression that pulmonary incompetence is always harmless in the absence of a high pulmonary vascular resistance

Idiopathic' dilatation of the pulmonary artery is occasionally due to the same abiotrophy that affects the ascending aorta in cases of Marfan s syndrome and in these rare cases has been known to rupture A good example of the double lesion is illustrated in fig 8 18

## EBSTEIN S DISEASE

A rare anomaly of which there were ten examples in the present series all diagnosed during life is malformation and displacement of the tricuspid valve (Ebstein 1866) With greater precision in diagnosis an increasing number of live cases are coming to light Helpful reviews are those by Yater and Shapiro (1937) Engle *et al* (1950) Baker *et al* (1950) and Medd *et al* (1954)

*Pathology*

The anterior cusp always retains some attachment to the annulus fibrosus but the posterior loses its connection entirely and is attached to the walls of the right ventricle (Brown 1950) The cusps themselves are also grossly malformed and present a curious basket like arrangement that is difficult to describe The right ventricle and atrium are grossly dilated the infundibulum distal to the valve usually less so The foramen ovale is patent and functions in varying degree in about two thirds of the cases

*Clinical features*

Males and females are affected equally There were six males and four females in the present series

Ages vary greatly according to the severity of the lesion and range from early childhood to 80 The ages of my patients when first seen were 13 15 25 28 18 months 14, 4 5 22 and 53

Symptoms are remarkably mild in relation to the size of the heart shadow radiologically and have been overrated in the literature Cyanosed cases have gravitated to special clinics in the hope of obtaining relief by means of cardiac surgery and after an unsuccessful operation or otherwise have tended to find their way into the medical press Thus the general impression seems to be that Ebstein s disease is a cyanotic form of congenital heart disease yet of the ten new cases reported here only one presented as such although the patient herself denied it and only one of three other cases that I catheterised for my colleagues was centrally cyanosed clinically Many of these acyanotic cases are still being overlooked and continue to masquerade under a motley variety of diagnoses

Effort intolerance was negligible in four of my cases, slight (grade 1) in four and moderate (grade 2A) in the other two. None were in the least disabled except during attacks of paroxysmal tachycardia (*vide infra*). In the worse cases dyspnœa and fatigue limit physical activity.

Attacks of faintness accompanied by intense cyanosis are probably due to paroxysmal tachycardia but they are unusual. Baker *et al* (1950) found only two examples in some 25 clinical records in the literature. In a case that I observed intense cyanosis accompanied paroxysmal *nodal* tachycardia that caused giant venous cannon waves and obvious reversed inter atrial shunt (fig 6 33). With normal rhythm the venous pressure oscillated gently around sternal angle level (fig 8 22) and central cyanosis was only just apparent (denied by the patient).

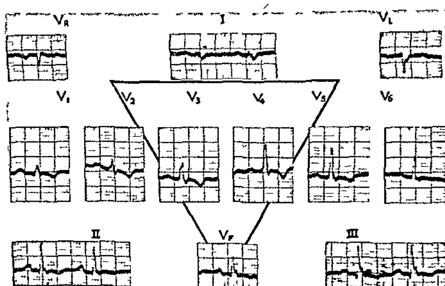



Fig 8 20—Electrocardiogram in Ebstein's disease showing a right bundle branch block pattern and rather low voltage

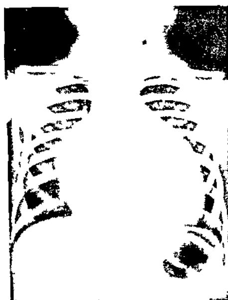
*Physical signs*

The physical signs are highly characteristic and together with the electrocardiogram and X ray appearances usually make the bedside diagnosis obvious.

1. Central cyanosis at rest, clubbing and polycythæmia *are usually absent*. Only one of my ten cases had these features. A second had doubtful cyanosis at rest but no clubbing. Three had a highly coloured moon facies, peripheral cyanosis and no clubbing. The other five looked entirely normal. The majority of cases in the literature have been cyanosed from birth or have developed cyanosis in childhood or adolescence. The discrepancy is attributed to selected material.

2 The peripheral pulse is usually small and the blood pressure rather low, figures around 110/80 being typical

3 The venous pressure and pulse are of two kinds they are either inconspicuous, the pressure being around or below sternal angle level with *a*, *c* and *v* of rather low amplitude (fig 8 22) or they have the features of tricuspid incompetence (fig 8 23) giant *a* waves were *not* seen in any of my cases and a moderate *a* wave about 3 mm Hg above *v*, in only two instances The literature is not at its best in respect of the clinical venous pulse in Ebstein s disease but on the whole the findings seem to have been similar





(a) Anterior view (b) Second oblique position

Fig 8 21—Typical skiagram in a case of Ebstein s disease showing gross dilatation of the right ventricle and atrium and clear lung fields

4 *The heart is quiet* On two occasions cases of pulmonary valve stenosis were referred as ? Ebstein s disease when there was a grade 3 right ventricular heave on another occasion a case of Ebstein s disease was referred as ? severe pulmonary valve stenosis when no cardiac impulse could be felt anywhere No convincing impulse could be felt over the right ventricle in any of these ten cases in one there was slight retraction A gentle localised left ventricular impulse was felt far out towards the axilla in at least three instances the point was not always recorded however—there was merely the statement that the heart felt unusually quiet

5 On auscultation most observers have commented on the frequency of gallop rhythm the extra sound being a right ventricular third heart sound Right atrial gallop is very unusual If the P R interval is prolonged right atrial contraction may accentuate the third heart sound

6 The moderately loud—presumably pansystolic—murmur that was heard over a wide area in about 80 per cent of cases in the literature accompanied by a thrill in three of my patients may be attributed to tricuspid incompetence

7 A very characteristic superficial diastolic scratch, giving the cadence of triple rhythm (disregarding the gallop sound) was heard in all but two cases in this series and has been mentioned in about half the recorded cases in which auscultatory details have been given It is usually heard best close to the sternum in the third left space, but in two of my cases it was louder *well to the right of the sternum* at the same level It sounds more like diastolic pericardial friction over the distended right atrium than a true intracardiac murmur occurring at a time when the right atrial pressure falls steeply maximal right atrial movement due to volumetric change provide a possible explanation but its exact mechanism awaits elucidation In two recent cases this diastolic murmur may well have been tricuspid for it was much accentuated during inspiration

*Electrocardiogram*

All observers have stressed the frequency of partial or complete *right bundle branch block*, which has been recorded in about 90 per cent of all cases There were no exceptions among the ten reported here The form of the complexes however is often a little bizarre as in the case illustrated (fig 8 20) and in eight out of the ten the voltage was low

*Tall sharp P waves* have been described in well nigh 80 per cent of published cases In the present series however P was inconspicuous (as in the illustration) in eight and prominent (3 or 4 mm high and 0 08 second wide) in two

The *P R interval* has been slightly prolonged (usually 0 24 sec ) in a little over one third of cases In the present series it ranged between 0 14 and 0 2 second in eight out of the ten cases and was 0 24 second in the other two

*X ray appearances*

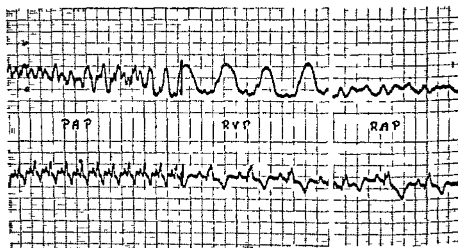
The radiological features of Ebstein s disease are as characteristic as the physical signs and the electrocardiogram The aorta is small and the lung fields clear and translucent The enormous relatively still heart shadow produces a sharp stencilled effect on the skiagram reminiscent of pericardial effusion (fig 8 21) the bulk of this shadow represents the distended right ventricle and atrium the former approaching the left lateral wall of the thorax the latter bulging far to the right

## *DIFFERENTIAL DIAGNOSIS*

Faced with such a characteristic picture made up of so many striking and unusual features it is difficult to think of any other possible diagnosis If the history gives no indication of the duration of the condition peri

cardial effusion might well be considered in acyanotic cases and was in fact the way one of my patients presented Like Ebstein's original case and five out of 28 reviewed by Baker *et al* (1950) this patient had pulmonary tuberculosis and the effusion had an all too ready explanation The Ebstein diastolic scratch lends superficial credence to such a diagnosis But the jugular venous pressure pulse the curious and unexpected gallop and the electrocardiogram should prevent error

In practice the commonest mistake has been confusion between Ebstein's disease and severe pulmonary valve stenosis with or without reversed interatrial shunt There is rarely much excuse for such an error for there are at least seven major points of difference (see pulmonary stenosis)




*Paper speed 25 mm sec*

Fig 8 22—Relatively normal intracardiac pressures in a case of Ebstein's disease

*Cardiac catheterisation*

I have personally catheterised seven cases of Ebstein's disease but do not propose to catheterise another willingly Three deaths due to catheterisation are known to me one being in the present series and paroxysmal tachycardia occurred in another of mine There need be no hesitation in using the catheter to disprove a case referred as Ebstein's disease if the real diagnosis is thought to be pulmonary valve stenosis on firm clinical grounds and the catheter can be used safely in the right atrium to check the possibility of pericardial effusion if there is any real doubt about the matter but in the great majority of cases the clinical diagnosis of Ebstein's disease is beyond question and should be left at that Of the ten cases in this series five were confirmed by means of catheterisation (two also at necropsy) and five have not yet been confirmed or catheterised but are still alive

The findings at catheterisation are as follows

1 All pressure pulses may be more or less normal but of rather low amplitude (fig 8 22) in the illustration the right atrial *c* wave is unduly prominent and has overcome the *x* descent This appears to be the rule

2 Right atrial and right ventricular pressure pulses are more or less indistinguishable and resemble right atrial tracings in gross tricuspid incompetence (fig 8 23)

According to Van Lingen (1952) it may be possible to locate the position of the tricuspid valve by demonstrating two ventricular chambers that portion proximal to the valve behaving like the right atrium that distal to the valve like a true ventricle

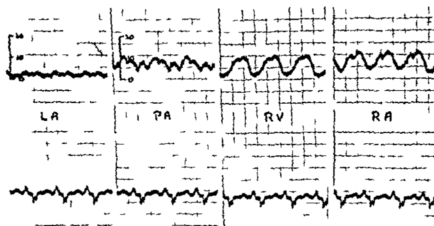



Fig 8 23 – Tricuspid incompetence type of pressure tracing in a case of Ebstein's disease showing an almost identical systolic pressure in the pulmonary artery right ventricle and right atrium

3 The pulmonary artery pressure which was recorded in five of my seven cases is normal but low the systolic level being the same as that in the right ventricle distal to the tricuspid valve

4 The arterial oxygen saturation varies greatly according to the degree of reversed interatrial shunt In the horizontal position it is usually between 70 and 90 per cent saturated In my five successfully catheterised cases it was 87 83 78 72 and 90 per cent saturated But it would be interesting to know what it was in the vertical position One of these cases was clinically cyanosed at rest and she was the only one with an oxygen capacity above 190 ml per litre The pulmonary blood flow in four adults was 6 4 4 4 3 1 and 5 3 litres per minute—the fifth patient (aged 4) did not have her oxygen uptake measured

5 The pulmonary capillary venous pressure measured in two cases was normal (fig 8 23) proving that in these two cases any opening in the atrial septum could have been no more than a small foramen ovale

*Prognosis and treatment*

Life expectancy varies with the degree of cyanosis the average age of death in cases cyanosed from birth is 12 years whereas in acyanotic cases it is over 28 years (Baker *et al* 1950) Patients who are symptom free and wholly acyanotic have a good chance of surviving to middle age or beyond No specific treatment is possible

## ATRIAL SEPTAL DEFECT

*Embryology* Atrial septal defect refers to a relatively large non valvular opening in the atrial septum, through which blood may flow either way. Embryologically the atrial septum is formed in the first place by the sickle shaped septum primum which grows forwards from the dorsal wall of the common atrium, dividing it into two For a time communication exists between the two atria in front of the crescentic edge of the growing septum If development is arrested at this stage a septal defect results and is situated in the lower anterior part of the septum just below and usually including part of the fossa ovalis When growth proceeds normally this hole is obliterated and a new one the foramen ovale appears in the upper and dorsal part of the septum primum arrest at this stage results in a defect just above the site of the fossa ovalis With further normal development the foramen ovale comes to lie more anteriorly and is turned into a valve by the growth of the septum secundum on the right side of the septum primum and covering it at all points except over the area known as the fossa ovalis When the septum secundum develops fully and the septum primum degenerates completely the defect occurs at the site of the fossa ovalis

In *patent foramen ovale* the septa are fully developed, but imperfectly fused When pressure is applied to the right side of the fossa ovalis the septa are parted, blood penetrates between them and escapes into the left atrium through the patency in the upper part of the septum primum known as the foramen ovale proper In fœtal life the relatively high pressure in the right atrium keeps the valve open and causes blood to be shunted from right to left in order to avoid the pulmonary circulation At birth the pressure rises in the left atrium and forces the septum primum against the septum secundum thereby closing the valve In 80 per cent of all individuals fusion then takes place between the two septa and the foramen ovale is permanently closed In the remaining 20 per cent fusion fails and valvular patency continues It is then a potential cause of reversed interatrial shunt if for any reason the pressure in the right atrium comes to exceed that in the left This may happen in such conditions as pulmonary hypertension pulmonary stenosis and pulmonary embolism

A cardiac catheter may slip through a patent foramen ovale into the left atrium without difficulty and may enter the left ventricle (fig 8 24) or any of the pulmonary veins (fig 8 25) or the left atrial appendage (fig 8 26) The pressures and electrical potentials in these chambers may thus be



8 24—Catheter n the left entricle via a patent foramen ovale



Fig 8 5—Catheter in a pulmonary vein via a patent foramen o ale

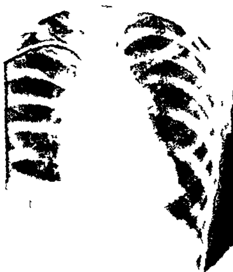


Fig 8 6—Catheter in l ft atrial appendag

obtained in favourable cases including otherwise normal hearts The mean left atrial pressure is about 4 mm. Hg higher than the right Pulmonary venous samples have usually been around 96 per cent saturated with oxygen Uncomplicated patent foramen ovale is easily distinguished from atrial septal defect because of the absence of any appreciable inter atrial shunt as judged by samples from both atria and their respective venous systems

*Hæmodynamics* An atrial septal defect is usually 1 to 3 cm in diameter and carries a considerable shunt from left to right atrium, the right ventricle offering less resistance to filling than the left Oxygenated blood is thus added to the normal intake of the right ventricle the stroke output of which is correspondingly increased The shunt results in enlargement of the right atrium and ventricle dilatation of the pulmonary artery and pulmonary plethora Left atrial leakage deprives the left ventricle of its full intake, the left ventricular stroke output is diminished, the left ventricle and aorta hypoplastic and the pulse small Progressive right ventricular enlargement eventually leads to failure the pressure in the right atrium then rises and if it exceeds that in the left the shunt is reversed and cyanosis develops As a rule, however, the left atrial pressure also rises with heart failure and shunt reversal is prevented this may be due to a reversed Bernheim effect or to the pressure equalising influence of a stretched pericardium According to some authorities a high jugular venous pressure in A S D means left ventricular failure Cyanosis in A S D nearly always means an extreme pulmonary vascular resistance (see Eisenmenger s syndrome)

*Incidence* A S D accounted for 18 per cent of the author s series of 900 cases of congenital heart disease It shows a slight preference for females, the sex ratio being 3 2 in their favour The average age for the whole group was 23 years The number per cent in each decade was as follows

| Age | 1–10 | 11–20 | 21–30 | 31–40 | 41–50 | 51–60 | 61–70 |
|---|---|---|---|---|---|---|---|
| No per cent | 19 | 38 | 15 | 12 5 | 7 | 5 | 3 5 |

The oldest was 68 and the oldest on record 82 (Ellis Greaves and Hecht 1950)

*Associated lesions* Arachnodactyly high arched palate alone or obvious thoracic deformity alone (usually kyphoscoliosis or pigeon chest) occurred with equal frequency in one quarter of the cases Coincident mitral stenosis (Lutembacher 1916) whether congenital or acquired was recognised clinically in only two instances and discovered at operation in another it is difficult to understand the high incidence of Lutembacher s syndrome in past necropsies Bedford Papp and Parkinson (1941) for instance, put it at 25 per cent Current opinion has swung sharply away from this concept and finds support in modern figures concerning its frequency at post

mortem e g 6 per cent in the series reported by Nadas and Alimurung (1952)

## CLINICAL FEATURES

### Symptoms

The majority of uncomplicated cases of atrial septal defect have no symptoms This statement applied to 57 per cent of the author s series Effort intolerance was slight in 12 5 per cent moderate in 12 5 per cent considerable in 6 per cent and gross (total incapacity) in 12 per cent Of those with grade 3 or 4 effort intolerance 55 per cent were between the ages of 43 and 68 (average 55 5), of the remainder one third were infants

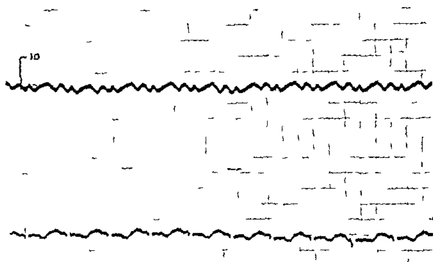


Fig 8 27—Normal right atrial pressure oscillating gently around zero in a case of A S D

one third ordinary severe cases in younger adults and one third owed much of their disability to other lesions such as emphysema polycystic kidney or mitral stenosis It follows that symptomless uncomplicated atrial septal defect in young adults is a relatively benign anomaly

Recurrent bronchitis or bronchopneumonia occurred in 10 per cent of all cases and was attributed to the tendency of already hyperæmic lungs to react excessively to minor respiratory infections

Hæmoptysis occurred in only 3 per cent and bronchial tuberculosis was responsible for the hæmorrhage in two of these cases

### Physical signs

Patients with atrial septal defect are not infrequently under developed frail or gracile in build and any of the associated congenital anomalies mentioned above may be present

The *peripheral pulse* is characteristically small The *jugular venous pressure* was strictly normal in 75 per cent of the series reported here (fig 8 27) slightly raised (about 3 cm above the sternal angle) with *a* and *v* more or less equal in amplitude in 17 per cent and high with a wave form suggesting tricuspid incompetence in 8 per cent The *right atrial pressure pulse* was recorded in 58 cases and confirmed these clinical observations Neither giant nor dominant *a* waves were seen in uncomplicated cases nor was *v* in any way remarkable except in those with tricuspid incompetence

*The left ventricle is nearly always impalpable* but a substantial systolic lift over the *hyperdynamic right ventricle* from the left sternal edge to the mid clavicular line or beyond is almost invariable *Pulmonary artery pulsation* in the second left space can be felt in 50 per cent of cases

There are several important auscultatory signs A *pulmonary ejection murmur* due to an increased pulmonary blood flow was heard in 80 per cent of the series and was accompanied by a thrill in one quarter of all cases When the thrill was very pronounced catheterisation or other physical signs usually demonstrated coincident pulmonary stenosis and such cases have been excluded from the group under consideration A pulmonary ejection click was heard occasionally but was unusual in the absence of a high pulmonary vascular resistance or slight pulmonary stenosis A *pulmonary diastolic murmur* due to functional pulmonary incompetence (Graham Steell murmur) was rare in the absence of pulmonary hyper tension but a soft *mid diastolic murmur*, usually in the third or fourth left space near the sternal edge or towards the apex of the right ventricle was heard in 30 per cent, This mid diastolic murmur which is accentuated during inspiration is attributed to turbulence set up at the defect itself or to a torrential tricuspid blood flow necropsies have disproved its mitral origin (except in Lutembacher s syndrome) The *second heart sound is widely split* and varies very little if at all with respiration The second or pulmonary element may be a little accentuated but is more often normal unless there is pulmonary hypertension The wide split was attributed by Barber Magidson and Wood (1950) either to right bundle branch block or to delayed emptying of the overfilled right ventricle perhaps to both Earlier closure of the pulmonary valve has been noted after successful repair of atrial septal defect without significant change in the electrocardiogram and right ventricular pressure curves timed against the electrocardiogram prove that there is no delay in the onset of right ventricular contraction (Leatham and Gray 1955) it follows that the wide split must be due to prolongation of right ventricular systole (or shortening of left ventricular systole) Failure of the split second heart sound to widen on inspiration was first noticed by Mr W W Dicks the senior cardiological technician at the London Hospital and was confirmed by Sowers (1952) and by Leatham and Gray (1955) we have assumed that the greatly distended right ventricle is unable to fill much more on inspiration, or that



Fig. 8.28—Skiagram of a case of atrial septal defect showing dilatation of the pulmonary artery and its branches, enlargement of the right ventricle and atrium, and hypoplasia of the aorta



(a) Antero-posterior view



(b) First oblique position showing dilatation of the left atrium

Fig. 8.29—Lutembacher's syndrome

the increased inspiratory flow from the systemic veins into the right atrium tends to inhibit the shunt proportionally

Fluoroscopy in well developed cases (fig 8 28) reveals gross dilatation and conspicuous pulsation (hilar dance) of the pulmonary artery and its branches peripheral pulmonary plethora enlargement of the right atrium and ventricle and hypoplasia of the aorta and left ventricle (Bedford Papp and Parkinson 1941) In Lutembacher s syndrome (fig 8 29) the left atrium is also enlarged In less advanced cases however and especially in children the changes described may be much less noticeable (fig 8 30)



Fig 8 30 —Atrial septal defect in a child aged 10

Electrocardiograms show a partial or complete right bundle branch block pattern in 95 per cent of cases (fig 8 31) (Barber Magidson and Wood (1950) The prolonged activation of the right ventricle is almost certainly due to dilatation of that chamber and not to any real interruption of the right bundle branch The secondary R wave in lead $V_1$ seldom exceeds 10 mm in height in uncomplicated cases and is usually well under this The P wave was normal under 2 mm in height in 90 per cent of the present series when it is tall and sharp associated pulmonary stenosis or a high pulmonary vascular resistance should be suspected A slightly prolonged P R interval (around 0 24 sec ) was seen in 10 per cent Atrial fibrillation occurred in 10 per cent of the whole series and was closely related to age thus it was found in only one patient under 30 years old in 12 5 per cent of those between 30 and 50 in 50 per cent of those between 51 and 60 and in 80 per cent of those over 60 years

The diagnosis may be proved by obtaining samples of relatively oxygenated blood from the right atrium, right ventricle, and pulmonary artery by means of cardiac catheterisation when samples from the venæ cavæ show ordinary venous blood (Howarth McMichael and Sharpey Schafer 1947) In 86 cases investigated at the Institute of Cardiology samples obtained from the right atrium right ventricle and pulmonary artery differed little and ranged between 75 and 90 per cent saturated with oxygen caval samples being normal (55 to 75 per cent saturated) Samples from the left atrium left ventricle and femoral artery were normal (94 to

96 per cent saturated) in about half the cases and between 84 and 93 per cent saturated in the other half According to Swan Burchell and Wood (1954) slight shunt reversal can usually be demonstrated by means of dye concentration curves especially when the dye is injected into the inferior vena cava and they think this explains the slightly reduced arterial oxygen saturation not infrequently found But in 12 cases in the present series pulmonary venous samples* were obtained and proved to be similarly unsaturated in five of them suggesting that hurry through a widely dilated pulmonary vascular bed may also be responsible In uncomplicated atrial

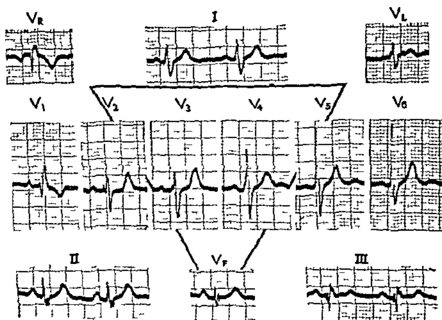



Fig 8 31—Electrocardiogram in a case of A S D showing a partial right bundle branch block pattern

septal defect the pulmonary blood flow is usually two to three times the systemic flow, i e about 10 to 15 litres per minute The systemic flow is commonly normal but may be reduced in severe cases

Pressure tracings from the two atria usually show little actual difference (fig 8 32) the potential gradient from left to right being masked by the flow It is assumed that the normal difference between left and right atrial pressure is due to greater resistance on the part of the left ventricle to

* In taking pulmonary venous samples the vessel must not be blocked by the catheter or the sample is bound to be 99 to 100 per cent saturated When a pulmonary vein is blocked the distal pressure rises sharply until it equals the pulmonary artery pressure and the tracing becomes arterial in form

diastolic filling i e to a higher diastolic tone in the left ventricle than in the right The greatest shunt flow may therefore occur during the period of rapid ventricular filling immediately after the opening of the tricuspid valve

The pulmonary artery pressure was normal or only slightly raised in 90 per cent of these cases and between 60/30 and 100/50 in 10 per cent excluding 15 cyanotic cases with an extreme pulmonary vascular resistance and reversed inter atrial shunt which are considered later in relation to Eisenmenger s syndrome It is clear that the normal long term reaction of the pulmonary arterial tree to the increased blood flow is vasodilatation This prevents any serious rise of pressure with flows up to 15 litres per

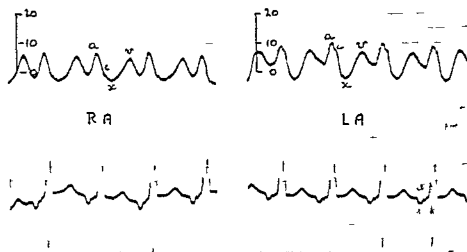



Fig 8 3.—Left and right atrial pressure tracings in a case of A S D showing a slightly higher pressure on the left side although the R A P is raised secondary to heart failure

minute (in an adult) with flows greater than this relatively harmless hyperkinetic pulmonary hypertension occurs without an increased pulmonary vascular resistance Over the years secondary vascular changes may increase the resistance a little but never seriously In 20 per cent of cases however the reaction is of an entirely different order in these the pulmonary vascular resistance is high being 5 to 9 units in the group discussed here (about half of the 20 per cent) and 10 to 20 units in those with reversed shunt This vasoconstrictive response seems to be determined at birth and is discussed more fully in connexion with Eisenmenger s syndrome

## COMPLICATIONS

*Pulmonary hypertension* complicating atrial septal defect as described above may be recognised by exaggeration of the *a* wave of the jugular pulse a more sustained left parasternal heave a pulmonary ejection click

closer splitting of the second heart sound and obvious accentuation of the second or pulmonary element free pulmonary incompetence greater dilatation of the pulmonary artery less pulmonary plethora with loss of peripheral arterial tapering, and the development of a tall sharp P wave in standard leads and of a higher voltage secondary R wave in lead $V_1$ of the electrocardiogram If the pressure in the right atrium comes to exceed that in the left central cyanosis develops and the peripheral pulmonary vascular shadows diminish

*Tricuspid incompetence* may result from gross dilatation of the right ventricle with or without pulmonary hypertension and is usual when there is *congestive failure* It is remarkable that the shunt does not usually reverse

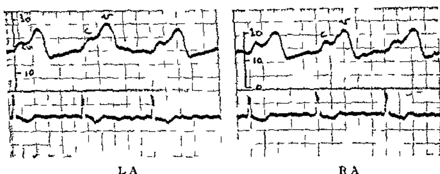



Fig 8 33—Pressure tracings from both atria in a case of A S D showing a slightly higher pressure on the left side despite marked tricuspid incompetence and a very high right atrial pressure

in such cases despite right atrial pressures of 10 to 20 cm above the sternal angle That the left atrial pressure remains higher than the right even under these circumstances (fig 8 33) demands some special *mechanism* which increases the resistance to left ventricular filling Whether this is a reversed Bernheim effect a manifestation of left ventricular failure or due to the pressure equalising influence of a stretched pericardium is as yet uncertain

*Pulmonary stenosis* complicates atrial septal defect in about 10 to 15 per cent of cases It may be very mild and may hardly alter the physical signs or the haemodynamics but an impressive systolic thrill over the pulmonary artery is suggestive and a pulmonary artery pressure at least 10 mm Hg lower than that in the right ventricle is diagnostic

*Severe pulmonary stenosis* associated with atrial septal defect causes reversal of the interatrial shunt and a cyanotic form of congenital heart disease (q v )

*Partial anomalous pulmonary venous drainage* into the right atrium (q v ) is *not* uncommon and increases the left to right shunt

*Bacterial endocarditis* is very rare in uncomplicated cases of atrial septal defect (about 1 per cent) and its occurrence at once suggests associated pulmonary stenosis

*PROGNOSIS*

Of the 167 cases in this series five died naturally—three (aged 2 3 and 43) from congestive failure one from associated cor pulmonale and one from polycystic kidneys Five others died from attempted surgical repair all advanced cases and one (also in failure) died as the result of cardiac catheterisation The average age of these 11 patients (6 6 per cent of the series) was 21

According to McGinn and White (1933) and Roesler (1934) the average age of death in atrial septal defect is 35 to 36

On the whole however it is believed that the prognosis in uncomplicated cases with average shunts is good congestive failure being a late development and not to be expected before middle life This must influence selection of cases for surgical treatment

*TREATMENT*

Over the past few years a determined attempt has been made to find the best method of closing atrial septal defects Murray (1948) passed fascia lata sutures through the atrial septum in such a way as to occlude the defect but the method was too uncertain to be followed up Bailey (1953) closed many defects by suturing part of the wall of the distended right atrium to the interatrial septum making sure that free passage was preserved between the mouths of the venæ cavæ and the tricuspid orifice This technique has been used by many surgeons with considerable success but lacks the precision of direct suture Gross (1952 1953) showed that atrial septal defect could be closed by direct suture if a leak proof rubber well was first attached to the right atrial wall when the right atrium is opened blood rises in the well to a level which represents the central venous pressure and so maintains normal right ventricular filling and allows the surgeon to perform his task under water as it were Air embolism is avoided because the tricuspid valve is totally immersed The introduction of open heart surgery however made possible by hypothermia or crossed circulations has resulted in the modern method of closing the defect by simple suturing under direct vision (Lewis and Taufic 1953 Swan *et al* 1953) Subsequent physiological studies have proved that the defect remains closed (Blount *et al* 1954)

Eighteen of the present series were operated on six by Mr W C Cleland using Bailey s technique and twelve by Sir Russell Brock with the aid of hypothermia Although six of these patients died they were very advanced and the results in the survivors have been most gratifying

At the present time surgical repair should be recommended if the pulmonary blood flow is more than three times the systemic flow if the pulmonary vascular resistance is between 6 and 10 units or if there is obvious tricuspid incompetence or congestive heart failure Until the mortality rate is under 5 per cent uncomplicated cases with good effort

tolerance and 2 to 1 shunts should certainly be left alone With bidirectional shunt it is reasonable to advise repair *as long as the pulmonary blood flow is still increased* even though the pulmonary vascular resistance is above 10 units (800 dynes sec /cm$^5$) for the resistance may be expected to fall if the flow can be diminished but it is not reasonable to advise repair when an extreme resistance has resulted in a normal or reduced pulmonary blood flow and reversed shunt

## PERSISTENT COMMON ATRIOVENTRICULAR CANAL

A common atrioventricular opening with deformed mitral and tricuspid valves is always associated with a persistent ostium primum (A S D) usually with a ventricular septal defect and often with mongolism

Of 55 cases reviewed by Rogers and Edwards (1948) over half died within the first year of life and only five survived to the age of 30

Clinically these cases usually present with all the features of an exceptionally large atrial septal defect complicated by mitral (as well as tricuspid) incompetence an appreciable number however have the Eisenmenger reaction and reverse the shunt

## PARTIAL ANOMALOUS PULMONARY VENOUS DRAINAGE

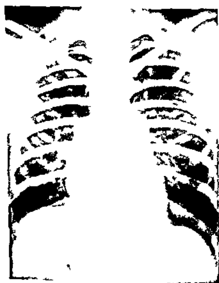


Fig 8 34—Skiagram showing an anomalous pulmonary vein joining the right atrium

One or more pulmonary veins may drain directly into the azygos superior vena cava right atrium or inferior vena cava According to Brody (1942) anomalous pulmonary veins are twice as frequent in the right lung as in the left A left to right shunt at caval or atrial level occurs and results in a physiological situation similar to that found in atrial septal defect with which it is not infrequently associated In isolated cases the shunt is relatively small and the condition may be only recognised as a result of a routine skiagram (fig 8 34) The anomalous vessel is commonly dilated and shows up well in tomograms (fig 8 35) A cardiac catheter may enter such a vessel directly from the superior vena cava (fig 8 36) inferior vena cava or right atrium and may be filled with contrast medium so that its course may be seen more clearly or



(a) Anterior view



(b) Lateral tomogram

Fig 8 35—Anomalous right pulmonary venous drainage into the azygos vein

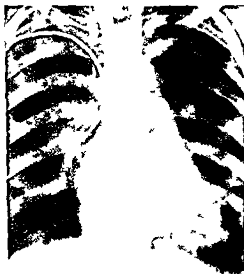


Fig 8 36—Skiagram showing a catheter lying in an anomalous pulmonary vein joining the superior vena cava

diaginol may be injected directly into the pulmonary artery through a No 9 catheter so as to delineate the whole course of the vessel

When anomalous pulmonary venous drainage is associated with atrial septal defect it may be important to know how much blood is being shunted through each If the anomalous vein joins the azygos or either vena cava this can be learned easily enough by analysing samples obtained from the vena cava above and below the entrance of the vessel and from the right atrium if it joins the right atrium however the shunt is more difficult to estimate but comparison of time concentration curves recorded by means of an ear oximeter after the injection of 30 mg of Evans blue dye first into one pulmonary artery and then into the other may help when the injection is made on the side of the anomalous pulmonary veins the left to right shunt is greater than when it is made on the contralateral side and the quantitative difference between the two curves represents the magnitude of the venous shunt

### *TREATMENT*

It is rarely necessary to interfere with partial anomalous pulmonary venous drainage because the shunt carried is usually too small to cause any trouble and the prognosis excellent (Smith 1951) Transplantation may have to be considered however in exceptional cases and if there is a suitable pulmonary vein on the same side direct venous anastomosis can be performed

## VENTRICULAR SEPTAL DEFECT

Ventricular septal defect commonly refers to an isolated defect of the membranous part of the interventricular septum due to failure of the aortic septum to fuse with the ventricular septum Diagnosed clinically for the first time by Roger (1879) the lesion has been said to account for 35 to 37 per cent of all cases of congenital heart disease recognised at school age (Perry 1931 Muir and Brown 1934) Such high figures probably include many instances of aortic stenosis simple pulmonary stenosis infundibular stenosis and mitral incompetence

### *NOMENCLATURE*

The term maladie de Roger, if used at all, should be reserved for those mild cases of ventricular septal defect that conform to Roger s original description, i e to about one third of pure uncomplicated cases (Wood Magidson and Wilson 1954) The remainder have so many characteristic features denied by this description that they have no right to the title Nor is Taussig s classification of ventricular septal defect into high (severe) and low (mild) types justified for in 90 per cent of cases the defect whether

severe or mild is located in the anterior part of the membranous septum (Selzer 1949)

## *INCIDENCE*

In the author s series of 900 virtually proved cases of congenital heart disease ventricular septal defect occurred in its pure uncomplicated form in 8 per cent as part of Eisenmenger s complex in 3 per cent in association with simple pulmonary stenosis in 1 3 per cent and as part of Fallot s tetralogy or pulmonary atresia in 12 7 per cent thus in one form or another ventricular septal defect was found in one quarter of all cases The present section deals only with uncomplicated ventricular septal defect

The sex ratio in this series was equal, as it was in the 92 post mortem cases mostly collected from the literature by Selzer (1949)

The average age of the 72 cases described here was 12 7 years and the percentage in each decade as follows

| 0–10 | 11–20 | 21–30 | 31–40 | 41–50 | 51–60 years |
|---|---|---|---|---|---|
| 51 | 31 | 10 | 5 | 2 | 1 |

## *HÆMODYNAMICS*

During systole from the shutting of the mitral and tricuspid valves to well after aortic valve closure the high pressure gradient across the ventricular septum ensures a left to right shunt The extra quantity of blood received by the right ventricle is pumped into the lungs and is received in due course by the left atrium and left ventricle Thus both ventricles and the left atrium do more than their normal share of work only the right atrium being spared As in atrial septal defect the pulmonary vascular resistance usually remains normal so that the pulmonary blood pressure only rises when the pulmonary blood flow approaches or exceeds 15 litres per minute (hyperkinetic pulmonary hypertension) The systemic output is maintained as near to normal as possible and the arterial blood is adequately saturated with oxygen

## *CLINICAL FEATURES*

### *Symptoms*

Cases of mild or moderate severity have no symptoms but when the shunt is considerable patients are usually under developed and may complain of breathlessness palpitations and recurrent attacks of bronchitis In severe cases congestive failure must be expected sooner or later and is not infrequent in childhood (Marquis 1950)

### *Physical signs*

The *facies* is normal or lean never bloated By definition all uncomplicated cases are acyanotic

The *peripheral pulse* is small when the shunt is relatively large normal in the maladie de Roger

The *jugular venous pressure and pulse* are normal unless there is heart failure

A *hyperdynamic left ventricular thrust* at the apex beat and a *lift over the right ventricle* near the left sternal border can both be felt as a rule and pulsation over the pulmonary artery in the second left space occurs in a quarter of the cases Only in the maladie de Roger is the cardiac impulse normal

Roger (1877) accurately described the *characteristic murmur* as surprisingly loud extending right through systole covering both heart sounds

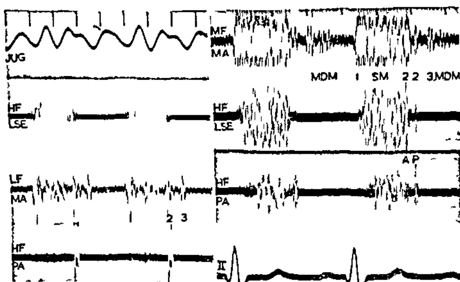



Fig 8 37—Phonocardiogram illustrating the pansystolic murmur of V S D with a simultaneous jugular phlebogram

Fig 8 38—Phonocardiogram showing a functional mitral diastolic murmur (top tracing) in a case of V S D

HF high frequency MF medium frequency LF low frequency LSE left sternal edge MA mitral area PA pulmonary area

*I k  uledg ent t D  I b y L  th m*

and with its maximal intensity over the upper third of the precordial region and chiefly median This loud pansystolic murmur (figs 8 37 and 8 38) was heard in 95 per cent of the present series usually in the 3rd and 4th left spaces near the sternal edge and was accompanied by a *thrill* in four fifths of them The murmur was soft in 3 per cent and absent altogether in 2 per cent A functional *mitral diastolic murmur* (fig 8 38) indistinguishable in timing quality intensity and duration from the Carey Coombs murmur of active rheumatic carditis was heard in precisely half the cases This murmur was noted by Laubry and Pezzi (1921) and may be attributed to a torrential mitral blood flow (Wood 1950) It is present in 90 per cent of severe cases 60 per cent of those with moderate shunts and 10 per cent of mild cases (Wood *et al* 1954) A *Graham Steell*

murmur due to functional pulmonary incompetence was heard in 14 per cent chiefly in those with pulmonary hypertension

The *second heart sound* when not obscured by the murmur is split normally or rather closely the pulmonary element is only accentuated in those with pulmonary hypertension The third heart sound is usually accentuated owing to rapid ventricular filling (fig 8 37)

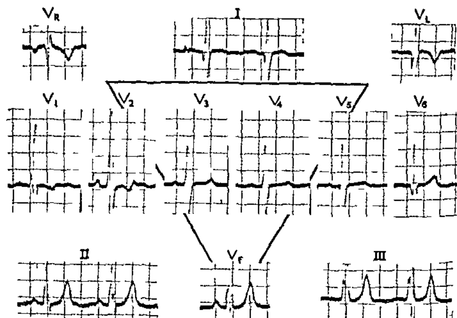



Fig 8 39—Electrocardiogram in a case of V S D showing an RSR complex in lead $V_1$ indicating right ventricular dilatation and a conspicuous Q wave in leads $V_6$ and $V_L$ pointing to a powerful left ventricle as well

*Electrocardiogram*

The electrocardiogram is normal in the maladie de Roger In those with moderate or large shunts the appearances vary according to the pulmonary vascular resistance when this is low good Q waves and large R waves in leads $V_5$ and $V_6$ with or without depression or inversion of T or U and deep S waves in leads $V_1$ and $V_2$ confirm the left ventricular enlargement and dominance the pattern resembling that seen in patent ductus when the resistance is raised however a conspicuous secondary R wave is seen in lead $V_1$ and a terminal S wave in lead $V_6$ the graph resembling that seen in atrial septal defect In the majority of cases however a variable mixture of these two types of graph is seen good Q waves in leads $V_5$ and $V_6$ emphasising the presence of a vigorous left ventricle and secondary R waves in lead $V_1$ proclaiming right ventricular enlargement as well (fig 8 39)

*Skiagram*

In mild cases the appearances are normal (fig 8 40) In the majority however radiology reveals a small aorta a variable degree of dilatation of the pulmonary artery and its two main branches (with or without hilar dance), pulmonary plethora hyperdynamic enlargement of both ventricles and slight dilatation of the left atrium (fig 8 41)



Fig 8 40—Maladie de Roger—X ray appearances



Fig 8 41—Skiagram of a case of ventricular septal defect with considerable increase of pulmonary blood flo

*Differential diagnosis*

The maladie de Roger is frequently confused with mild pulmonary valve stenosis simple infundibular stenosis acyanotic Fallot s tatralogy mild aortic stenosis and innocent left parasternal murmur whatever that may be

*Mild pulmonary valve stenosis* should be distinguished by the higher position of the thrill and murmur wide splitting of the second sound and post stenotic dilatation of the pulmonary artery

*Mild infundibular stenosis* with its low thrill and murmur and normal pulmonary artery is very difficult to distinguish from the maladie de Roger unless delayed pulmonary valve closure can be recognised

*Acyanotic Fallot s tetralogy* usually causes moderate effort intolerance even squatting in some cases and a clear single second heart sound in all other respects it may closely resemble maladie de Roger

*Mild aortic stenosis* should be recognised by the aortic ejection click and by the geography and timing of the aortic systolic murmur (q v )

murmur due to functional pulmonary incompetence was heard in 14 per cent chiefly in those with pulmonary hypertension

The *second heart sound* when not obscured by the murmur is split normally or rather closely the pulmonary element is only accentuated in those with pulmonary hypertension The third heart sound is usually accentuated owing to rapid ventricular filling (fig 8 37)

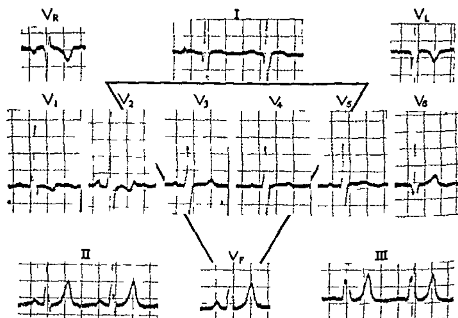



Fig 8 39—Electrocardiogram in a case of V S D showing an RSR complex in lead $V_1$ indicating right ventricular dilatation and a conspicuous Q wave in leads $V_4$ and $V_L$ pointing to a powerful left ventricle as well

*Electrocardiogram*

The electrocardiogram is normal in the maladie de Roger In those with moderate or large shunts the appearances vary according to the pulmonary vascular resistance when this is low good Q waves and large R waves in leads $V_5$ and $V_6$ with or without depression or inversion of T or U and deep S waves in leads $V_1$ and $V_2$ confirm the left ventricular enlargement and dominance the pattern resembling that seen in patent ductus when the resistance is raised however a conspicuous secondary R wave is seen in lead $V_1$ and a terminal S wave in lead $V_6$ the graph resembling that seen in atrial septal defect In the majority of cases however a variable mixture of these two types of graph is seen good Q waves in leads $V_5$ and $V_6$ emphasising the presence of a vigorous left ventricle and secondary R waves in lead $V_1$ proclaiming right ventricular enlargement as well (fig 8 39)

proved at operation and in consideration of the technical errors involved in sampling it is clear that defects measuring less than 2 mm in diameter and passing shunts of less than 1 litre per minute would not be detected with ordinary routine methods of investigation It must be admitted therefore, that a pansystolic left parasternal murmur with entirely normal physiological findings could well be due to a minute ventricular septal defect for necropsies have certainly proved the existence of such minute defects This does not mean however that the maladie de Roger is common after all because the majority of cases so labelled on traditional evidence have been proved by modern techniques to have a different explanation for the murmur

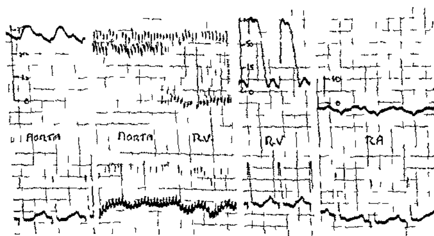



Fig 8 42—Pressure pulses from a case of ventricular septal defect with hyperkinetic pulmonary hypertension at systemic level the pulmonary blood flow was 20 L min and the resistance 3 units

In one third of the mild cases there was a significant difference between infundibular and low right ventricular samples the former resembling samples from the pulmonary artery the latter samples from the right atrium this difference was very rarely found in moderate or severe cases

The pulmonary vascular resistance was raised moderately in half the severe cases There is good evidence that the size of the defect is not directly responsible for the behaviour of the small pulmonary vessels in these instances (see Eisenmenger s complex) but it was never smaller than the critical 1 cm in diameter Severe cases without a raised resistance are apt to die of left ventricular failure or bronchopneumonia in childhood for there is then little to prevent an intolerable shunt The pulmonary blood pressure alone gives little indication of the resistance and may even reach systemic level when the resistance is normal if the shunt is large enough (fig 8 42) This may be called hyperkinetic pulmonary hypertension

## COMPLICATIONS

*Eisenmenger's complex* (q v ), which may be defined as pulmonary hyper tension with bidirectional or reversed interventricular shunt usually occurs when the pulmonary vascular resistance lies between 10 and 20 units

*Complete heart block* occurred in only one of the 72 cases recorded here Conversely when ventricular septal defect had been diagnosed elsewhere in several cases of congenital heart block no shunt could be demonstrated by means of cardiac catheterisation and careful auscultation supported by phonocardiography usually proved that the systolic murmur on which the diagnosis had been based was in fact an aortic or pulmonary ejection murmur Functional mitral incompetence may also mislead

*Bacterial endocarditis* was the cause of death in 22 per cent of the 80 necropsied cases reviewed by Selzer (1949) Its true incidence is difficult to assess frequency rates as high as 57 per cent being recorded in post mortem material (Gelfman and Levine 1942 Welch and Kinney 1948) and as low as 1 per cent in clinical series (Perry 1937 Muir and Brown 1934 Wood *et al* 1954) perhaps 10 to 20 per cent would be near the truth Vegetations form on the right ventricular side of the septum around the defect and on the opposite wall of the right ventricle where the shunted blood stream impinges Emboli are confined to the pulmonary circulation and may cause subacute or recurrent hæmorrhagic pulmonary inflam mation or infarction

*Pulmonary or infundibular-stenosis* with normal aortic root and left to right shunt may be associated with ventricular septal defect (Abrahams and Wood 1950) the combination occurring in 1 5 per cent of all cases of congenital heart disease (Wood *et al* 1954) When the stenosis is mild it is usually overlooked until demonstrated by means of cardiac catheterisation when it is relatively severe the ventricular septal defect is usually over looked clinically Cases with bidirectional or reversed shunt are indistin guishable from Fallot s tetralogy

*Aortic incompetence* the anterior cusp being prolapsed into the defect (fig 8 43) or tethered towards the defect by a fibrous band (Laubry and Pezzi 1921) occurs in about 2 per cent of cases (Wood Magidson and Wilson 1954) The combination may be mistaken for patent ductus and so lead to fruitless thoracotomy

## PROGNOSIS

During the seven year period in which these 72 cases of isolated un complicated ventricular septal defect have been studied none have died of the lesion But there were only three patients over 40 years old whereas 15 5 per cent of patients with atrial septal defect were over 40 Again 29 per cent of 88 fatal cases collected by Selzer (1949) died during the first year of life and another 20 per cent between the ages of 1 and 5 The

average age of death in Abbott's series was 14, the oldest being 49. It is clear, therefore, that ventricular septal defect is a serious anomaly, patients often dying from congestive failure in early childhood (Baldwin, Moore and Noble, 1946), and it is only the mild maladie de Roger that has a good prognosis. The only risk in these mild cases is bacterial endocarditis, and with modern treatment this can usually be cured.

There have been some interesting cases in which characteristic signs of a ventricular septal defect discovered in childhood have disappeared with advancing years. Whilst it is difficult to prove that these were not examples of innocent left parasternal murmur, it has been suggested that spontaneous obliteration of small defects may sometimes occur (Parkes Weber, 1918).

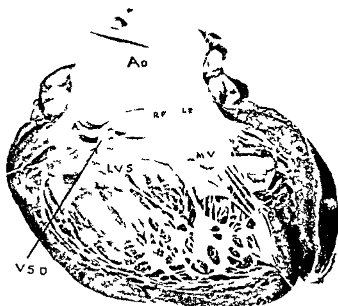



Fig. 8.43—Photograph of specimen from a case of aortic incompetence complicating V.S.D.; the anterior aortic cusp is prolapsed into the defect.

[illegible]

## TREATMENT

No reparative treatment is yet available, but Murray (1948) first made the attempt. Mild cases should be encouraged to lead normal unrestricted lives, but severe cases need care and should limit their physical activities. Dental treatment, sore throat and other pyogenic infections should be covered by a short course of penicillin to prevent endocarditis.

## PATENT DUCTUS ARTERIOSUS

### EMBRYOLOGY

In fœtal life the ductus arteriosus joins the root of the left pulmonary artery to the aorta at a point immediately distal to the left subclavian artery and it is a short muscular vessel 1 cm or so in length and about as wide as the great vessels which it joins In the unaerated lung of the fœtus the pulmonary capillaries and arteries are practically shut down and offer a resistance to flow that is much higher than the systemic resistance mixed venous and placental blood from the right ventricle therefore passes directly from the pulmonary artery into the descending aorta At the same time mixed venous and placental blood which has passed through the foramen ovale is pumped by the left ventricle into the ascending aorta Although further mixing undoubtedly takes place in the arch of the aorta on the whole left ventricular blood passes to the head and upper extremities while right ventricular blood passes to the trunk and lower extremities It should be clearly understood that the systolic pressures in the two ventricles and great vessels are identical the ventricles are subjected to the same filling pressure and work against the same total peripheral resistance

At birth aeration of the lung is followed by a rapid decline in pulmonary vascular resistance alveolar oxygenation discouraging pulmonary vaso constriction Within three hours of birth blood sent to the right arm is over 90 per cent saturated with oxygen whereas blood sent to the legs is still partly venous from the end of the third hour the pulmonary vascular resistance gradually falls below systemic level the process being completed in normal individuals by the end of the third day after which arterial samples from the arms and legs are the same (Eldridge Hultgren and Wigmore 1954) The duct itself normally closes by some inherent process within the first six weeks after birth

### INCIDENCE

Patent ductus was the chief or sole lesion in 9 2 per cent of Abbott s 1 000 collected cases of congenital heart disease and accounted for 13 per cent of my own 900 an additional 2 per cent having reversed shunt

The sex ratio is 7 3 in favour of females (Gross 1952) there were 78 females and 37 males in the present series

In the 115 cases reported here the average age was 17 and the percentage distribution per decade as follows

| Age | 0–10 | 11–20 | 21–30 | 31–40 | 41–50 | 51–60 |
|---|---|---|---|---|---|---|
| No per cent | 36 | 32 | 15 | 9 5 | 6 5 | 1 |

### HÆMODYNAMICS

Since the systemic peripheral resistance is normally about eight times the pulmonary, the shunt in uncomplicated patent ductus is from aorta to pulmonary artery The total systemic resistance is lowered by the leak from the aorta arterial blood enters the pulmonary circulation the total

pulmonary blood flow is increased and the left atrium and left ventricle have to deal with the augmented flow the total blood volume is raised (Cassels and Morse, 1947) Hyperkinetic pulmonary hypertension may occur with large shunts as with atrial septal defect and ventricular septal defect but the pulmonary vascular resistance is not ordinarily raised High pulmonary resistances around 15 units (systemic level) occur in 10 to 15 per cent of cases and may result in reversed shunt (see Eisenmenger's syndrome) Included in the present section is a small group (7 per cent) in which the pulmonary resistance is moderately raised but insufficiently so to prevent a predominant aorto pulmonary shunt

## CLINICAL FEATURES

There are no symptoms in mild or moderate cases In severe cases with large shunts recurrent bronchitis and bronchopneumonia are common in childhood as with severe atrial septal defect and ventricular septal defect Physical development is usually poor palpitations and throbbing may be troublesome and there may be symptoms of left ventricular failure

### *Physical signs*

The *peripheral pulse* is water hammer in quality Corrigan's sign may be present in the neck and the diastolic blood pressure tends to be low according to the degree of aorto pulmonary shunt

The *venous pressure* is normal in uncomplicated cases but may be raised a little if the pulmonary vascular resistance is high or as a result of an increased blood volume

The *cardiac impulse* is left ventricular in type and hyperdynamic Medial retraction over the right ventricle confirms that the left ventricle is alone enlarged Pulsation in the second left space over the pulmonary artery may be appreciated when the shunt is large or when there is a raised pulmonary vascular resistance

On *auscultation* the chief sign is the classical machinery murmur of Gibson (1900) it is usually heard best in the first or second left interspace is more or less continuous waxes towards the end of systole wanes in mid diastole and is accompanied by a thrill in two thirds of cases It may be absent in infancy although it has been recorded as early as the sixth week (Adler 1953) This typical murmur was heard in 95 per cent of the present series The murmur was systolic only in two cases with gross shunt in one trivial case and in two with a raised pulmonary vascular resistance which was insufficient to prevent an aorto pulmonary shunt A continuous murmur was never heard in the pulmonary hypertensive cases with reversed shunt In difficult ca es a doubtful Gibson murmur may be brought out by any device that increases total flow (such as exercise) or that increases the pressure gradient across the duct (such as Muller's experiment)

The *second heart sound* was usually difficult to analyse clinically in view of the loud coincident bruit but phonocardiography showed that aortic

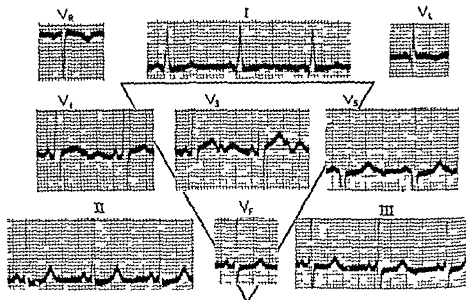



Fig 8 44—Electrocardiogram in a case of patent ductus showing left ventricular enlargement There is a strong QR pattern with inverted U waves in lead V5

valve closure was delayed in cases with large shunt A often falling after P the split being reversed (Gray 1955) The phenomenon was attributed to delayed emptying of an overfilled left ventricle

A *pulmonary diastolic murmur* due to functional pulmonary incompetence was recognised in 8 per cent In the group with pulmonary hypertension and reversed shunt (discussed later) it was heard in 70 per cent

A *functional mitral diastolic murmur* due to a torrential mitral blood flow was detected in 39 per cent of all uncomplicated cases it was present in 87 per cent of those with large shunts and in one third of those with

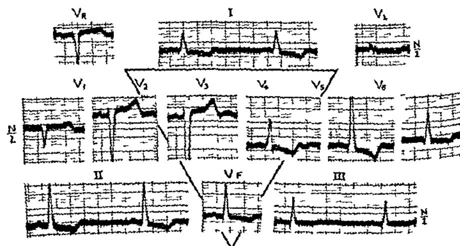



Fig 8 45—Gross left ventricular preponderance in a case of patent ductus

moderate shunts but never in mild or trivial cases It commonly disappeared after ligation of the duct this rapid flow murmur was never heard in the true pulmonary hypertensive group

*Electrocardiogram*

The electrocardiogram is normal in mild cases and usually normal in cases of moderate severity but when the shunt is large prominent Q waves unusually tall R waves and perhaps inverted U waves in leads V and $V_6$ confirm the enlargement of the left ventricle (fig 8 44) and in the most florid cases the T waves may be inverted in left ventricular surface leads or their equivalents (fig 8 45) In striking contrast to atrial septal defect no case of patent ductus had a partial right bundle-branch block pattern

*Radiological appearances*

Skiagrams (figs 8 46 and 8 47) reveal pulmonary plethora dilatation of the pulmonary artery enlargement of the left ventricle and slight dilatation of the left atrium (Donovan Neuhauser and Sosman 1943) A conspicuous hilar dance is unusual and the right branch of the pulmonary artery is rarely impressive The aorta in patent ductus is not so small (fig 8 48) as in atrial septal defect and ventricular septal defect and may be more pulsatile The right ventricle and atrium are strictly normal in uncomplicated cases Rarely a comma shaped arc of calcium can be seen in the ductus or in the wall of the left pulmonary artery opposite to the opening of the ductus

A local bulge in the region of the aortic isthmus can be demonstrated by means of angiocardiography in a limited number of cases and is thought to represent the widened mouth of the ductus or possibly a traction aneurysm of the aorta (Steinberg Grishman and Sussman 1943) A characteristic filling defect at the top of the left pulmonary artery has been described by Goetz (1951) With suitable technique angiocardiograms may also show the pulmonary artery filling twice first from the right ventricle then from the aorta Retrograde aortography offers an alternative means of obtaining good angiograms



Fig 8 46—Skiagram of a case of patent ductus showing enlargement of the left ventricle but little dilatation of the pulmonary artery




Fig 8 47—Skiagram of a more advanced case of patent ductus showing considerable left ventricular enlargement and engorgement of the pulmonary vessels in addition to dilatation of the pulmonary artery

*PHYSIOLOGICAL FINDINGS*

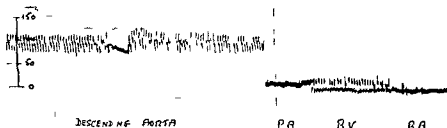
The diagnosis may be proved in doubtful cases by means of cardiac catheterisation. Samples of blood from the superior vena cava, right atrium and right ventricle are normal (about 70 per cent saturated) whereas samples from the pulmonary artery are usually 80 to 85 per cent saturated. Slight admixture of arterial blood in right ventricular samples may be found when there is functional pulmonary incompetence.

In the present series 61 cases were catheterised, about a third of them in each group of severity. In mild cases the pulmonary blood flow measured about 1.5 times the systemic flow and in three instances no shunt at all could be demonstrated, even in one catheterised twice. At operation in these mild cases the duct did not exceed 0.6 cm in external diameter.



Fig 8.48—Skiagram of a case of patent ductus showing a prominent aortic knuckle in addition to dilatation of the pulmonary artery and pulmonary plethora

In the moderate group the pulmonary blood flow was 2 to 2½ times the systemic flow, being commonly around 10 to 12 litres per minute. The pulmonary blood pressure and vascular resistance were normal (fig 8.49) and at operation the duct usually measured from 7 to 12 mm in external diameter.



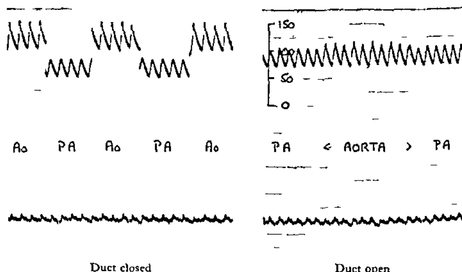

*Time marking 1 and 5 sec*

Fig 8.49—Pressure pulses from the descending aorta and pulmonary artery in an uncomplicated case of patent ductus showing a steep pressure gradient between the two

In the severe cases with normal resistances the pulmonary blood flow averaged 3.5 times the systemic flow, ranging between 12 and 30 litres per minute. Hyperkinetic pulmonary hypertension was demonstrated in

all but two of these cases the average pressure being 55/35 mm Hg and the range from 32/15 to 75/55 The pulmonary vascular resistance was normal averaging 2 units, the range being 0 5 to 4 The pulmonary blood pressure never quite reached systemic level at rest in this group but approached it very closely in several instances as a result of temporary stress and would presumably do so also on exercise At operation the duct was always more than 1 cm in external diameter

The arterial oxygen saturation was normal for catheter conditions (90 to 97 per cent) in 88 per cent of all these cases and between 87 and 89 per cent in the remainder




Duct closed Duct open

*Time marking 0 2 and 1 0 sec*

Fig 8 50—Case of patent ductus with hyperkinetic pulmonary hypertension together with a moderately raised pulmonary vascular resistance when the ductus was open the pulmonary artery pressure was 10 mm Hg lower than the aortic when the ductus was closed the aortic pressure rose from 115 to 150 mm Hg and the pulmonary artery pressure fell from 105 to 83 mm Hg

Finally there was a small group (5 per cent) of severe cases in which the pulmonary vascular resistance was raised (5 to 9 units) but in which the shunt was still unidirectional or predominantly from aorta to pulmonary artery Although the ductus itself was about 1 cm in diameter the raised resistance prevented a large shunt the average pulmonary blood flow being barely twice the systemic flow The pulmonary blood pressure was more or less at systemic level (fig 8 50) These cases are not yet in the Eisenmenger group but could become so

By repeatedly guiding the tip of the catheter from the left to the right pulmonary artery and back again the ductus was sooner or later entered in one third of the last 42 cases catheterised As it passes through the duct the catheter lies at the level of the left pulmonary artery, with the subaortic window above it (fig 8 51) The tip nearly always passes straight

down the descending aorta very rarely into the left subclavian artery When a catheter passes through an aorto pulmonary window its course up the ascending aorta and round the arch is higher as can be demonstrated by superimposing on the skiagram a second film with the catheter lying in the left pulmonary artery Again in the anterior view a catheter passing through a duct and down the descending aorta usually curves backwards in a medial direction (fig 8 63) whereas a catheter passing up the ascending aorta and round curves backwards in a left lateral direction (fig 8 101) in other words the former tends to loop anticlockwise the latter clockwise



Fig 8 51—Skiagram in the second oblique position showing a catheter passing through a patent ductus down the descending aorta the sub aortic window lies above the catheter

## *DIFFERENTIAL DIAGNOSIS*

Errors in the diagnosis of patent ductus arteriosus fall into four main groups

1 *Mistaking other continuous murmurs for Gibson s murmur*

A *jugular venous hum* can be abolished at once by compressing the jugular veins at the root of the neck

*Pulmonary atresia with a broncho pulmonary anastomosis* may cause a continuous murmur on either or both sides but such cases are cyanotic and patent ductus with reversed shunt causing cyanosis loses the Gibson murmur

*Arterio venous fistula* in the left upper lobe of the lung may cause a continuous murmur under the left clavicle but the skiagram should reveal the opacity and if the lesion is of any size there should be central cyanosis *Coronary arterio venous fistula* causes a machinery murmur at a lower level and the skiagram may show a calcified aneurysm A *congenital arterio venous angioma* in the thoracic wall is very rare and unlikely to be in the right place to cause confusion

*Perforation of an aortic sinus* into the pulmonary artery secondary to bacterial endocarditis and therefore usually with aortic incompetence as well may be very confusing In the only case I have seen, which was presented to me as a recanalised duct (for the [illegible] ad the ligamentum arteriosum ligated) the gross water [illegible] blood

pressure 180/40) and greatly enlarged and hyperdynamic left ventricle were out of proportion to the relatively slight degree of pulmonary plethora and the 2 1 shunt demonstrated by cardiac catheterisation

An *aorto pulmonary septal defect* is clinically indistinguishable from patent ductus, for physiologically it is identical It is likely to be encountered in 1 to 2 per cent of all cases submitted for ligation The machinery murmur may be exceptionally loud and perhaps a little low and central but little confidence can be placed on minor differences of this kind If a catheter can be passed through the communication its course may settle the question failing that retrograde aortography or selective dye concentration curves may solve the problem But on the whole it may be more economical to accept the slight risk of diagnostic error and to proceed as if any aorto pulmonary shunt were due to patent ductus for such an assumption will save 98 patients out of 100 much discomfort Aorto pulmonary septal defects may themselves be repaired but require the help of hypothermia or some form of temporary artificial circulation

2 *Mistaking certain combinations of murmurs for Gibson s murmur*

*Ventricular septal defect with aortic incompetence* has often been mistaken for patent ductus not only because the combined murmurs have been misinterpreted but also because of the water hammer pulse predominant hyperdynamic left ventricle functional mitral diastolic murmur and pulmonary plethora Nevertheless this is an error that should not be made for the two or three murmurs present do not make the Gibson murmur and the degree of water hammer pulse and left ventricular enlargement are disproportional to the amount of plethora

*Combined mitral and aortic incompetence* in children without a rheumatic history may also confuse experienced cardiologists again because the combination of murmurs superficially resembles the Gibson murmur and because of the water hammer pulse predominant and hyperdynamic left ventricle and short mitral diastolic murmur But there is no pulmonary plethora—only pulmonary venous congestion—and the murmurs should not really be mistaken for Gibson s murmur

3 *Mistaking other members of the plethoric group for patent ductus*

The difficulty here is only encountered in relation to patent ductus without a continuous murmur The syndrome includes a pulmonary systolic murmur perhaps a Graham Steell murmur a hyperdynamic enlarged left ventricle a functional mitral diastolic murmur and pulmonary plethora Possible causes include ventricular septal defect patent ductus and persistent truncus A small pulse right ventricular dilatation as well as left pansystolic murmur close but normal splitting of the second sound and diminutive aorta favour ventricular septal defect Central cyanosis of course at once distinguishes persistent truncus but failing that there is still the loud single second sound and the prominent

aorta Patent ductus without a continuous murmur is suggested by a water hammer pulse pure left ventricular enlargement and reversed splitting of the second sound

Despite these considerations real difficulty in accurate bedside diagnosis often arises and is not always resolved by means of cardiac catheterisation although theoretically the physiological data should be conclusive

*(c) Difficulty with the Eisenmenger syndrome*

Cases with pulmonary hypertension due to an extreme pulmonary vascular resistance (average 17 units) and reversed aorto pulmonary inter ventricular or interatrial shunt are very difficult to sort out at the bedside and will be discussed fully later (see Eisenmenger s syndrome) Fortunately at the present time the distinction between these three conditions is purely academic

## ASSOCIATED ANOMALIES AND COMPLICATIONS

Although patent ductus may be associated with almost any other congenital anomaly in clinical practice it usually occurs alone the more common associated lesions include *coarctation of the aorta* as already described and *tricuspid atresia* In the latter the ductus serves a useful purpose by providing a natural pathway whereby mixed venous and arterial blood can reach the lungs *Patent ductus is remarkably rare in any* form of pulmonary stenosis and I have not so far encountered it in otherwise uncomplicated atrial septal defect

Patent ductus may be associated by chance with certain acquired conditions such as rheumatic mitral valve disease and essential hypertension Organic *mitral incompetence* is seriously aggravated by the increased left ventricular stroke volume resulting from the shunt and provides a strong reason for ligating the ductus without delay although the result may be disappointing if the incompetence is already severe The effects of *mitral stenosis* are also seriously aggravated by the increased pulmonary blood flow resulting from the shunt and the combination calls for urgent *surgical treatment mitral valvotomy and ligation of the ductus may be* undertaken at the same operation In view of the serious consequences of coincident patent ductus and mitral valve disease active rheumatic carditis itself constitutes an important indication for advising early ligation *Essential hypertension* increases the aorto pulmonary shunt through a patent ductus and therefore puts a double load on the left ventricle on the other hand the aorto pulmonary communication lowers the total systemic resistance and tends to check the rise of blood pressure It is probably best to advise ligation of the ductus in these rare cases and to treat the increased hypertension that results by medical means

True complications of patent ductus include bacterial endarteritis heart failure functional mitral incompetence and pulmonary hypertension These are all discussed elsewhere

## PROGNOSIS

An appreciable number (perhaps 20 to 25 per cent) of cases of patent ductus die from left ventricular failure in infancy (Ziegler 1952) The average age of death was 24 in Abbott s post mortem series (1932) and 36 in a group of 60 cases reported by Shapiro and Keys (1943) The lesion is therefore not as benign as might be supposed The maximum age of survival so far recorded is 75 (Fishman and Silverthorn, 1951) The chief dangers are bacterial endarteritis and congestive heart failure Bacterial endarteritis occurred in 30 per cent of Abbott s series and in 37 5 per cent of those who survived early childhood Vegetations appear first at the pulmonary end of the ductus or on the opposite wall of the left pulmonary artery Spread to the heart valves (pulmonary aortic or mitral) occurs in 75 per cent of untreated cases (Vesell and Kross 1946)

Congestive heart failure occurred in 32 per cent of Abbott s 73 cases that survived infancy and in 30 per cent of 60 cases reported by Shapiro and Keys (1943) The gloomy prospects suggested by these reports are not entirely valid however for cases that come to necropsy are highly selected Clinical studies on unselected cases of patent ductus indicate a more favourable prognosis Thus Wilson and Lubschez (1942) followed 38 cases for an average period of 20 years during which there were no deaths from bacterial endocarditis or congestive failure Again Benn (1947) followed 30 cases for an average period of 8 years without meeting a single complication

## TREATMENT

Radical cure first achieved by Gross and Hubbard (1939) consists of ligation of the ductus or of excision of the ductus between ligatures and has proved very effective (figs 8 52 and 8 53) The most favourable age is between 6 and 10 Surgical treatment not only prevents bacterial endocarditis but usually cures this complication after its development (Touroff and Vesell 1940 Vesell and Kross 1946) Recanalisation is rare The total operative mortality is now 2 per cent and in uncomplicated cases only 0 5 per cent (Gross 1947 Crafoord 1948 Gross and Longino 1951) Of the author s cases 60 have so far been operated on without a death Bacterial endocarditis should be cured by means of penicillin if possible before submitting the patient to operation

### *Selection of cases for surgical treatment*

*Infants with large shunts* should have the ductus ligated and divided if possible without delay for the risk of early death from heart failure is considerable (Ziegler 1952) Indeed *all patients with large shunts* should be operated on without delay whatever the age at least up to the sixth decade

A *moderately raised pulmonary vascular resistance* (5 to 9 units) is a strong indication for surgical treatment for if the duct is not ligated the resistance




Fig 8 52—Case of patent ductus with large shunt

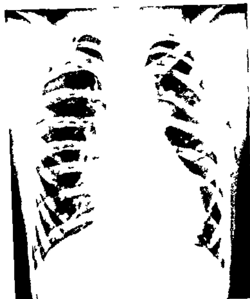


Fig 8 53—Same case one year after ligation

may be expected to reach systemic level sooner or later when it would be too late to help Surgery is contra indicated when the shunt is prevented or reversed by a pulmonary vascular resistance over 10 units Continued disregard for this rule has resulted in many deaths from unrelieved pulmonary hypertension then and there or within a year of the operation for without the duct there is no safety valve in the pulmonary circulation and the physiological situation becomes similar to that in primary pulmonary hypertension It is unreasonable to expect the resistance to fall after ligating the ductus when the pulmonary blood flow is already normal or diminished Surgery may still be advised however in cases of bi directional shunt if the pulmonary blood flow is increased

*Bacterial endarteritis* past or present provides strong grounds for ligation for infection is likely to be recurrent and on the next occasion may well prove fatal or do untold damage before being brought under control by means of antibiotics If bacterial endarteritis does not respond to medical treatment the operation should not be delayed for closure of the ductus alone cures the infection in two thirds of cases (Tubbs, 1944)

The only remaining question is whether or not to advise ligation in uncomplicated cases of mild or moderate degree In this group the surgical mortality is 0 5 per cent and the risk of subsequent bacterial endarteritis not less than 10 per cent at the most conservative estimate Since at least one fifth of cases of bacterial endocarditis prove fatal it follows that the immediate surgical risk is four times less than the ultimate risk of con servative management It is believed that this is not offset by the significant

difference between the words *immediate* and *ultimate* and that therefore all uncomplicated cases of patent ductus should be operated on, at least up to the age of 50 years

## EISENMENGER'S SYNDROME
## OR
## PULMONARY HYPERTENSION WITH REVERSED SHUNT

### DEFINITION

Eisenmenger's complex is ventricular septal defect with reversed shunt in the absence of pulmonary stenosis (Eisenmenger 1897) Until quite recently the reversed shunt was attributed to displacement of the root of the aorta to the right its position astride the defect seeming to favour reception of blood from both ventricles Eisenmenger himself was not responsible for this misconception and thought that any apparent over ride demonstrated at necropsy could be the result rather than the cause of the reversed shunt (Eisenmenger 1898) It is now known that the essential cause of the altered physiology in cyanotic cases of ventricular septal defect without pulmonary stenosis is a pulmonary vascular resistance more or less at systemic level The definition of Eisenmenger's complex therefore becomes *pulmonary hypertension with reversed interventricular shunt* Whether the aorta appears to ride over the defect or not is physiologically irrelevant

At the bedside and after viewing the electrocardiogram and skiagram it is usually easy enough to make a diagnosis of pulmonary hypertension with reversed or bidirectional shunt but often extremely difficult or impossible to determine the level of the shunt The term Eisenmenger syndrome has been used to describe this clinical picture (Wood 195 ) reserving the title Eisenmenger's complex to define a reversed shunt at ventricular level and there is something to be said for this attitude Alternatively the group as a whole might be called pulmonary hypertension with reversed shunt leaving the site of the shunt unspecified

### HÆMODYNAMICS

When the pulmonary vascular resistance is less than the systemic blood flows through a patent ductus or ventricular septal defect from left to right when the resistances are the same there may be no shunt at all and when the pulmonary resistance is higher the shunt is reversed This general law is not absolute for a shunt may occur at any time during the cardiac cycle but it is true enough as a working hypothesis To some extent it is also true for atrial septal defect although here there is obviously room for much greater variation for atrial pressures are only indirectly related to peripheral resistances

In patent ductus the reversed shunt is directed chiefly down the descending aorta so that the feet may be blue while the hands and face are pink (differential cyanosis) In ventricular septal defect and atrial septal defect with reversed shunt cyanosis is uniform

In patent ductus and ventricular septal defect with reversed shunt the systolic pressure in the pulmonary artery and right ventricle is always precisely the same as the systolic pressure in the aorta and left ventricle any potential pressure gradient between the two circulations being compensated for by the shunt flow This does not apply to atrial septal defect with reversed shunt in which the pulmonary artery pressure may be higher equal to or lower than the aortic in atrial septal defect also the pressure relationship between the two circulations may alter with changing conditions e g with exercise

When the shunt is wholly reversed the pulmonary blood flow is diminished the total systemic output remaining about normal

In patent ductus the left ventricular stroke volume is diminished by an amount equal to the shunt from pulmonary artery to descending aorta so that the right ventricle does the greater work the total resistance against which each ventricle is pumping being the same In ventricular septal defect the work of each ventricle is identical for although the left still receives a diminished amount from the left atrium its full quota is made up by the shunt at ventricular level In atrial septal defect with unidirectional reversed shunt the right ventricle pumps less blood than the left but if the pulmonary resistance is higher than the systemic it may have to do more work

On the whole the physiological situation is not bad The naturally high systemic resistance tends to prevent too great a right to left shunt at any level and so ensures a fair pulmonary blood flow at the same time the high pulmonary resistance is prevented from overburdening the right ventricle by the defect acting as a safety valve in the pulmonary circulation

The defect in Eisenmenger s complex is always 1 cm or more in diameter and *the high pulmonary resistance seems to be established at birth* Cases with ventricular septal defect of similar size in which the high fœtal pulmonary resistance falls to normal soon after birth run a serious risk of dying from heart failure in infancy It may be pointed out however that there is a well defined limit to the size of a left to right shunt when the pulmonary vascular resistance is normal the ceiling being reached when hyperkinetic pulmonary hypertension reaches systemic level Unfortunately the pulmonary blood flow has to be four to six times the systemic flow before this happens and few ventricles will tolerate such a burden It follows that in many cases the high pulmonary resistance of Eisenmenger s syndrome is life saving The ideal physiological reaction would be a pulmonary resistance of 5 to 6 units enough to ensure equalisation of pressures in the two circulations with moderate left to right shunts

Just what causes the high resistance is unknown Edwards (1950)

Civin and Edwards (1950 and 1951) originally suggested that it represented persistence of the fœtal type of pulmonary circulation in which a high resistance is maintained by thick muscular arteries, the object being to divert the blood flow from the lungs to the descending aorta via the ductus arteriosus Failure of this high resistance to subside when the lungs become aerated may be due to the hyperkinetic pulmonary hypertension that would occur at once if it did so in other words, pulmonary hypertension itself may be responsible for the vasoconstriction that maintains it Much the same idea was expressed by Soulie *et al* (1953) except that these authors blamed the riding aorta for the initial pulmonary hypertension —

## *INCIDENCE*

Pulmonary hypertension with bidirectional or reversed shunt through a patent ductus occurred in 2 per cent through a V.S.D. in 3 per cent and through an A S D in 1.5 per cent of the author s series of 900 cases of congenital heart disease Considering the relative frequencies of these three anomalies when uncomplicated (13 per cent 8 per cent and 18 per cent respectively) it may be seen that the Eisenmenger reaction occurred in 13 3 per cent of those with patent ductus 27 2 per cent of those with V S D and 7 7 per cent of those with A S D These rather startling differences are qualitatively just what might have been expected for of the three only atrial septal defect can be of unlimited size without necessarily endangering life and there are stricter limits to the size of a patent ductus than there are to the size of a ventricular septal defect In other words most cases of large atrial septal defect do not depend on the Eisenmenger reaction for their survival and there should be relatively more cases of ventricular septal defect of the necessary critical size than cases of patent ductus Swan *et al* (1953) found the same qualitative difference between the relative frequencies of raised resistances in these three conditions with direct left to right shunts still operating and pulmonary flows averaging twice the systemic flows the mean pulmonary artery pressure was above 40 mm Hg in 41 5 per cent of cases of patent ductus 70 per cent of cases of ventricular septal defect and only 5 per cent of cases of atrial septal defect

The *sex bias* when present was much the same as in uncomplicated cases of patent ductus V S D and A S D This denies the implication of the strong female sex factor operating in primary pulmonary hypertension

SEX RATIO

| | *Patent ductus* | | *V S D* | | *A S D* | |
|---|---|---|---|---|---|---|
| | M | F | M | F | M | F |
| Uncomplicated | 1 | 2 | 1 | 1 | 2 | 3 |
| Eisenmenger syndrome | 6 | 10 | 14 | 14 | 3 | 11 |

The *average age* of the patients with Eisenmenger s syndrome was also much the same as in uncomplicated cases of patent ductus and atrial septal

defect but was older in Eisenmenger's complex proper than in simple ventricular septal defect as shown in the table

| | AVERAGE AGE (years) | | |
|---|---|---|---|
| | *Patent ductus* | *V S D* | *A S D* |
| Uncomplicated | 17 | 12 7 | 23 |
| Eisenmenger syndrome | 16 | 2.. | 22 |

These figures help to show that *the high pulmonary vascular resistance of Eisenmenger's syndrome is not the end result of a direct shunt acting over a long period of time*

## *CLINICAL FEATURES*

Life long *effort dyspnœa* had limited physical activity in all but one of these 58 cases and had changed little through the years Those with atrial septal defect were most incapacitated averaging grade 3 (considerable) effort intolerance those with patent ductus were best averaging grade 2 effort intolerance while cases with ventricular septal defect fell midway between the two A history of *squatting* was obtained in 10 per cent but in none with patent ductus

*Angina pectoris* occurred in 10 per cent and was encountered equally in each group These six patients were all young adults aged 21 to 36 years and were no more cyanosed at rest than those without pain

*Syncopal attacks* also occurred in 10 per cent again with examples in each group They were usually provoked by effort and were associated with increased cyanosis None were fatal and they seemed neither as frequent nor as dangerous as in Fallot's tetralogy No opportunity to investigate the mechanism presented itself

*Recurrent hæmoptysis* was as frequent as angina pectoris and syncope but not more so The best examples were in older patients with either ventricular septal defect or atrial septal defect The cause of the hæmorrhage is obscure

*Central cyanosis* at rest usually dating from infancy (Donzelot *et al* 1949) was almost invariable in those with V S D (95 per cent) usual in those with A S D (75 per cent) and relatively uncommon with patent ductus (27 per cent) Even on effort one third of those with patent ductus remained acyanotic in the head and upper extremeties over half of them (57 per cent) however showed differential cyanosis at rest the face and hands being pink and the toes blue especially in a hot bath The idea that the onset of central cyanosis is typically late in Eisenmenger's syndrome occurring first around the age of puberty perhaps could not be substantiated although minimal cyanosis in childhood may certainly become more marked with advancing years Indeed, the sudden onset of dyspnœa and cyanosis in adults with a septal defect suggests some special reason for the sudden rise of pulmonary vascular resistance the two most likely

causes being multiple pulmonary embolism (especially in relation to pregnancy) and chronic bronchitis and emphysema *Clubbing of the fingers* was similarly most common in those with V S D (92 per cent) frequent enough with A S D (60 per cent) and least common in those with patent ductus (20 per cent) Clubbing of the toes alone was seen in two cases with patent ductus *Polycythaemia* (hæmoglobin over 15 G per cent) occurred in 85 per cent of the V S D cases 75 per cent of the A S D cases and 40 per cent of those with patent ductus Thus on all three counts in Eisenmenger s syndrome ventricular septal defect was associated with the greatest shunt reversal and patent ductus with the least while atrial septal defect occupied a middle position It must be said here however that this clinical conclusion was not confirmed by catheter studies for the arterial oxygen saturation averaged 80 per cent in those with V S D and 79 5 per cent in those with A S D with patent ductus it averaged 91 4 per cent in the right brachial artery and 81 2 per cent in the descending aorta

The *peripheral pulse* was usually small in those with A S D more often normal than small in those with V S D and either small or normal with patent ductus The pulse was normal in quality in all three groups

The *blood pressure* averaged 110 80 in those with A S D and 120/80 in those with V S D and patent ductus confirming the clinical impression of a smaller pulse when the shunt was at atrial level

The *jugular venous pressure* and pulse were normal in 60 per cent of all cases *a* was dominant usually measuring 3 mm Hg above *v* in 30 per cent and a large high pressure *v* wave due to heart failure or tricuspid incompetence was seen in 10 per cent Both conspicuous *a* waves and large *v* waves were relatively more common in cases with A S D than in the other two groups Giant *a* waves measuring more than 5 mm Hg were seen in only one instance

The *cardiac impulse* was impalpable in the region normally occupied by the left ventricle in one third of those with atrial septal defect and in two thirds of the other two groups the right ventricle occupied the apex beat in two thirds of those with atrial septal defect and in one third of the other two groups There was a conspicuous left parasternal heave over the hypertrophied right ventricle in half the atrial cases and in a quarter of the others while in the remainder the lift over the right ventricle was relatively slight and was absent altogether in 10 per cent of those with V S D and patent ductus In other words the right ventricle tended to be largest when the shunt was at atrial level *Pulsation over the pulmonary artery* itself was felt in three quarters of all cases

*Auscultation* revealed a systolic murmur over the right ventricular out flow tract and pulmonary artery in 82 per cent of all cases With A S D and patent ductus it was always an ejection murmur and usually followed a loud pulmonary ejection click with two exceptions it was loudest in the second or third left interspaces In one quarter of the cases with Eisen menger s complex proper however the murmur was loudest lower down

in the third and fourth spaces and may have been due to turbulence set up at the defect In two such instances the phonocardiogram showed it to be pansystolic A thrill accompanied the systolic murmur in one sixth of those with A S D one half of those with V S D and one quarter of those with patent ductus

The *second heart sound* was single or closely split (0 01 to 0 02 sec) with equal frequency in three quarters of the cases with V S D and obviously split (0 03 to 0 05 sec) in the remainder with patent ductus it was usually closely split and very rarely single with A S D it was obviously or even widely split (0 07 sec) in nearly half the cases and never single The pulmonary element of the second sound was nearly always loud unless pulmonary incompetence was severe

A *Graham Steell murmur* due to functional pulmonary incompetence was heard in two thirds of all cases and was equally frequent in each group

*Electrocardiogram*

*Auricular fibrillation* occurred in only two instances in a woman of 65 with atrial septal defect and a man of 62 with ventricular septal defect

*Complete heart block* occurred in two cases both with V S D

The *P wave* was extra sharp and measured 2 mm or more in amplitude (average 2 75 mm) in the most favourable lead in 56 per cent of cases with A S D or V S D but was normal in all but three cases with patent ductus in these three exceptions it measured only 2 mm in amplitude

*Considerable right ventricular preponderance* (grade 3 or 4) in chest leads was seen in 70 per cent of those with atrial septal defect and in *37 per cent* of those with ventricular septal defect or patent ductus its frequency being much the same in the last two groups *Normally balanced QRS T complexes* were never seen when the shunt was at atrial level but occurred in *16 per* cent of those with V S D *Right bundle branch block* was seen occasionally in each group (total 8 per cent)

*X ray appearances*

*Conspicuous dilatation of the pulmonary artery* was almost invariable it averaged grade 3 in those with A S D grade 2 in those with V S D and something between the two but nearer grade 3 in those with patent ductus

A *clear gap* or obvious concave recess *between the aortic knuckle and pulmonary arc* was rarely seen in cases with patent ductus (fig 8 54) but was well defined in about a quarter of those with Eisenmenger s complex or atrial septal defect (fig 8 55) A calcified arc identifying a patent ductus was seen only once The aortic knuckle was usually inconspicuous in all three groups but perhaps less so in those with patent ductus a prominent aortic knuckle was only seen in older subjects and then did not help to determine the site of the shunt

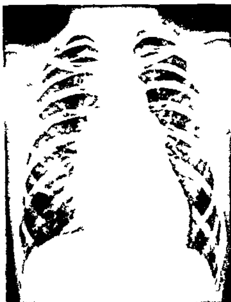


Fig 8 54—Case of pulmonary hypertension with reversed aorto pulmonary shunt through a patent ductus which can be seen as an abnormal convexity between the aortic knuckle and pulmonary arc



Fig 8 55—Case of pulmonary hypertension with reversed interatrial shunt showing a concave recess between the aortic knuckle and pulmonary arc

*Dilatation of the right ventricle and atrium* was most marked in cases with atrial septal defect and least evident in Eisenmenger s complex proper Thus in the former group grade 3 enlargement was recorded in two thirds of the cases whereas in the latter it was recorded in only 16 per cent Again the heart shadow was rarely normal in size when the shunt was interatrial whereas it was normal in 45 per cent of cases when the shunt was inter ventricular The average size of the heart shadow in cases with patent ductus lay midway between the two

The *peripheral pulmonary vascular markings* were light in nearly all cases (fig 8 56) in those with patent ductus or ventricular septal defect even the right main branch of the pulmonary artery was usually unimpressive only the left branch (left middle arc) being really conspicuous With atrial septal defect the proximal vessels tended to be heavier (fig 8 57)

A *right sided aortic arch* joining a right dorsal aorta occurred in 12 per cent of cases of Eisenmenger s complex proper (fig 8 58) but was never seen with A S D or patent ductus

*Angiocardiography*

In Eisenmenger s complex the ascending aorta and pulmonary artery opacify simultaneously from the right ventricle (fig 8 59) with atrial septal defect diaginol enters both atria and both ventricles more or less

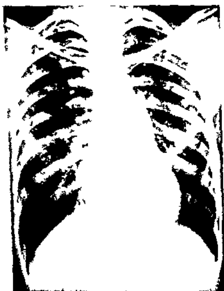


Fig 8 56—Eisenmenger s complex proper showing dilatation of th pulmonary artery and sl ght pulmonary ischæmia

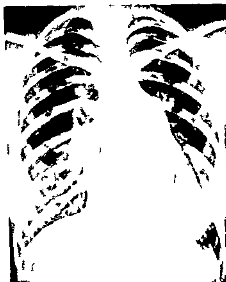


Fig 8 57—Eisenmenger s syndrome asso ciated with atrial septal defect showing considerable enlargement of the heart and dilatation of the prox mal branches of both pulmonary arteries the peripheral vascular shadows however are narrow

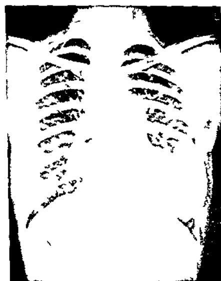


Fig 8 58—R ght s d d dorsal orta and dilatat on of the pulmon y artery in a cas of Eisenm nger s complex proper

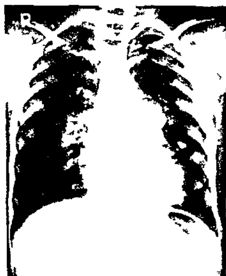


(a) Anterior view



(b) Second oblique position

Fig 8 59—Angiocardiogram in a case of Eisenmenger s complex proper showing simultaneous filling of the whole of the aorta and pulmonary artery mainly from the right ventricle although diaginol has also entered the left ventricle



(a) Anterior skiagram



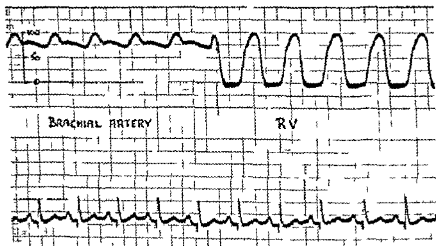
(b) Angiocardiogram showing opacification of the right side of the heart pulmonary artery and descending aorta the ascending aorta remaining translucent

Fig 8 60—Case of Eisenmenger s syndrome associated with patent ductus

simultaneously becoming much diluted in the process so that good contrast is more difficult to obtain with patent ductus the opaque medium enters the descending aorta from the pulmonary artery (fig 8 60)

*Dye concentration curves*

Evans blue dye injected selectively into the right ventricle through a cardiac catheter appears in the ear immediately in cases of Eisenmenger's complex its concentration being strongly fortified a few seconds later by dye that has passed through the lungs With atrial septal defect the initial hump is only seen when dye is injected into the right atrium and with patent ductus it is not seen at all in the majority of cases for little if any




*Pap r p d 25 mm s c* [illegible]

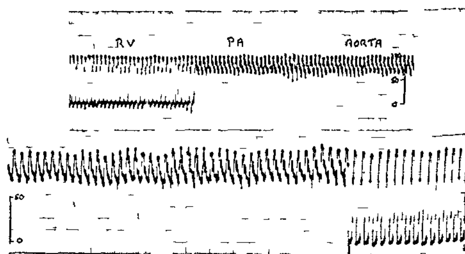
F g 8 61—Immediately consecutive pre sur tracing f om th [illegible] d right ventr cle in a ase of Eisenm nger s om pl x p p [illegible]

shunted dye enters the carotids on the other hand dye injected directly into the pulmonary artery appears at once in samples obtained from the femoral artery

*Cardiac catheterisation* usually reveals a *bidirectional shunt* at atrial ventricular or pulmonary artery level according to the site of the communication between the two circulations as pointed out by Bing *et al* (1947) In the present series the shunt was bidirectional in half the cases with atrial septal defect three quarters of the cases with ventricular septal defect and one third of the cases with patent ductus In three cases with patent ductus (18 per cent) there was *no shunt either way* but the catheter was passed through the duct and the systemic and pulmonary artery pressures were identical A perfectly balanced state of this kind was never

encountered with atrial or ventricular septal defect In the remainder of each group the *shunt was wholly reversed* The magnitude of the shunt was rarely great either way being usually of the order of 2–3 litres per minute The pulmonary blood flow averaged around 4 5 litres per minute in all groups With bidirectional shunts there was often very little difference between net systemic and net pulmonary blood flows but unidirectional reversed shunts naturally resulted in reduction of the pulmonary flow, which in such cases averaged 3 3 litres per minute

The *systolic pressure* in the two circulations was identical in all cases of Eisenmenger s complex (fig 8 61) and in all but one with patent ductus




*Paper speed 5 mm sec*

Fig 8 62—Immediately consecutive pressure tracings from the descending aorta and pulmonary artery in a case of Eisenmenger s syndrome associated with patent ductus

(fig 8 62) the *diastolic pressure* was also identical in nearly half these cases but when there was a difference the aortic diastolic pressure was usually higher than the pulmonary in Eisenmenger s complex and lower with patent ductus With atrial septal defect the systolic pressures in the two circulations were much closer than expected commonly within 5 mm Hg of each other the diastolic however was usually higher on the systemic side sometimes considerably so

The *pulmonary vascular resistance* averaged around 17 units in all groups the common range being between 13 and 22 units

In cases with patent ductus no difficulty was ever experienced in passing the catheter through it from the pulmonary artery to the descending aorta (fig 8 63) failure to do so under technically favourable conditions making the diagnosis virtually untenable In Eisenmenger s complex the ascending aorta was entered from the right ventricle in 40 per cent of cases, and with





(a) Anterior view (b) Second oblique position

Fig 8 63—Case of Eisenmenger's syndrome showing the usual lie of a catheter when it passes down a patent ductus into the descending aorta



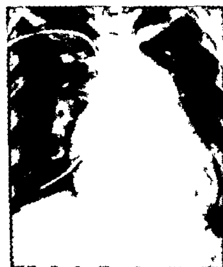


Fig 8 64—Case of Eisenmenger syndrome associated with atrial septal defect the catheter has passed through the defect and is lying in (a) the left upper pulmonary vein and (b) the left lower pulmonary vein

happened Clinically the physical signs were those of simple atrial septal defect apart from the cyanosis clubbing and polycythæmia

A somewhat similar situation arises in *cases having a common atrium* and in advanced atrial septal defect with right ventricular failure or tricuspid incompetence although reversal of the shunt does not occur at all readily in this latter group At the bedside the tell-tale signs of pulmonary hypertension are missing With a common atrium blood samples from all chambers and from both systemic and pulmonary arteries are similar Since the right ventricle offers less resistance to filling than the left the pulmonary blood flow is increased as in simple atrial septal defect unless the pulmonary vascular resistance is high

*Total anomalous pulmonary venous drainage into the right atrium* also suggests atrial septal defect with reversed shunt but without pulmonary hypertension This is discussed fully later

2 *Transposition of the great vessels with patent septa* If there is a high pulmonary vascular resistance the physiological situation is very like Eisenmenger s complex a bidirectional shunt taking place at ventricular level and the systolic pressure in the two circulations being identical but pulmonary artery samples are more saturated with oxygen than aortic samples since the former derive chiefly from the left ventricle and the latter from the right




Fig 8 65—Skiagram of a case of anoxic cor pulmonale due to emphysema complicating atrial septal defect with direct left to right shunt

*Persistent truncus arteriosus* with the pulmonary arteries arising from the root of the aorta is physiologically like Eisenmenger s complex only when the pulmonary vascular resistance is high Radiologically the aortic root is unduly prominent however and although the left branch of the pulmonary artery may be conspicuous the main pulmonary trunk is absent The diagnosis may be proved by angiocardiography or cardiac catheterisation as described later

3 *Primary pulmonary hypertension* with late reduction of arterial oxygen saturation to around 80 per cent may be distinguished by its relatively short duration (usually less than two years) rapid development of heart failure marked peripheral cyanosis giant *a* waves in the jugular pulse right atrial gallop frequent absence of a pulmonary systolic murmur

tall P pulmonale and gross right ventricular preponderance electrocardiographically angiocardiography shows no right to left shunt and cardiac catheterisation no left to right shunt the pulmonary artery pressure is usually lower than the systemic at rest and higher on effort

4 *Anoxic cor pulmonale* with secondary pulmonary hypertension and a normal or reduced cardiac output can usually be recognised by the history and the presence of advanced emphysema When the causal bronchitis and emphysema complicate atrial septal defect bedside diagnosis can be very difficult (fig 8 65) Catheterisation however then reveals a unidirectional shunt from left to right atrium and pulmonary venous samples as unsaturated as those from the left atrium left ventricle and systemic arteries as in the case illustrated which was later confirmed at necropsy

## *PROGNOSIS*

Of 35 fatal cases of Eisenmenger s complex reported in the literature and reviewed by Selzer and Laqueur (1951) 8 died in infancy 4 between the ages of three and ten and 5 7 7 1 and 3 in each subsequent decade respectively the oldest being 60 Figures for pulmonary hypertension with reversed interatrial or aorto pulmonary shunt should not be dissimilar and since ages are always younger in necropsy series it follows that on the whole the prognosis is fair The ages of the patients in the present series (tabulated earlier) confirm this view

## *TREATMENT*

Surgical repair of the defect is contra indicated in all forms of the Eisenmenger syndrome because it not only fails to relieve the pulmonary hypertension but also removes the safety valve in the pulmonary circulation It must be clearly understood however that pulmonary hypertension due to a raised pulmonary vascular resistance is no bar to ligation of a patent ductus or repair of an atrial septal defect if the pulmonary blood flow is still elevated i e if the left to right shunt is still dominant for the resistance may be expected to fall if the pulmonary blood flow can be reduced to normal *Surgical correction of central cyanosis is not the therapeutic objective in Eisenmenger s syndrome and if performed can only be regarded as a cosmetic operation which endangers life*

# PULMONARY STENOSIS

## *CLASSIFICATION AND FREQUENCY*

| ACYANOTIC *Normal aortic root* | | CYANOTIC *Dextroposed aortic root* | |
|---|---|---|---|
| Simple (with closed septa) | | Fallot s tetralogy | |
| valvular | 10% | chiefly valvular | 4% |
| infundibular | [illegible] | chiefly infundibular | 7% |

| | | | |
|---|---|---|---|
| With direct left to right shunt via | | (pulmonary atresia 1 7%) | |
| | | *Normal aortic root* | |
| patent ductus | rare | Pulmonary stenosis with reversed shunt | |
| V S D | 1 3% | interventricular | rare |
| A S D | 2% | interatrial | 3% |

Anatomically and embryologically the fundamental difference between the two main types of pulmonary stenosis depends on the position of the aortic root in simple stenosis whether the septa are patent or not the aortic root is normal and arises wholly from the left ventricle posteriorly and to the left in Fallot s tetralogy it is dextroposed and arises partly from the right ventricle so that it sits astride the interventricular septum which is necessarily defective In the former the pulmonary artery completely covers the root of the aorta crossing over it anteriorly from right to left in the latter the root of the pulmonary artery is displaced to the left and posteriorly so that it may not cover the aorta at all the origins of the two vessels tending to lie side by side the aorta on the right the pulmonary artery on the left

In simple stenosis the stricture is valvular in 80 per cent and infundibular in 20 per cent in Fallot s tetralogy it is mainly valvular in 40 per cent and mainly infundibular in 60 per cent In valve stenosis the cusps are fused or represented by a conical membrane with a small circular hole in the centre In fundibular stenosis a small chamber the primitive bulbus cordis (Keith 1909) is separated off from the body of the right ventricle by a fibrous ring which is the seat of the obstruction

Physiologically Fallot s tetralogy is pulmonary stenosis with reversed interventricular shunt and the only difference between it and simple pulmonary stenosis with ventricular septal defect is the degree of stricture which is sufficient to reverse the shunt in the former and usually insufficient to do so in the latter In relatively mild cases of Fallot s tetralogy and in severe cases after infundibular resection the shunt may be wholly from left to right despite the over riding aorta again in simple stenosis with ventricular septal defect the shunt may be reversed if the stricture is tight enough

## PULMONARY STENOSIS WITH NORMAL AORTIC ROOT

### *INCIDENCE*

Of all cases of congenital heart disease only atrial septal defect (18 per cent) is more common than pulmonary stenosis with normal aortic root (16 per cent excluding cases in which associated atrial septal defect or ventricular septal defect is dominant)

The sex ratio was unity in the series analysed here

The age distribution was as follows

| Age | 0–10 | 11–20 | 21–30 | 31–40 | 41–70 |
|---|---|---|---|---|---|
| No per cent | 38 | 35 | 19 | 5 | 3 |

It was more or less similar in all sub groups The oldest patient in the series was 67

## HÆMODYNAMICS

Pulmonary stenosis obviously interferes with the free passage of blood to the lungs and to overcome the obstruction the right ventricle must contract more powerfully This is achieved by hypertrophy and increased diastolic stretch The right atrium helps by contracting more strongly and forcibly distending the right ventricle at the end of diastole (fig 2 22) A giant *a* wave in the jugular pulse right atrial gallop and a tall P pulmonale are manifestations of this atrial contribution

In mild cases normal pulmonary artery pressures and flows are easily maintained with right ventricular systolic pressures of only 25 to 50 mm Hg (at rest) When the stricture is moderate satisfactory pulmonary artery pressures and flows can still be maintained with right ventricular systolic pressures of 50 to 100 mm Hg In severe cases, however the cardiac output is low and fixed and the pressure in the pulmonary artery is low despite systolic pressures in the right ventricle between 100 and 300 mm Hg Peripheral vasoconstriction helps to maintain the systemic blood pressure

In these severe cases the resistance of the stenosis is greater than the peripheral systemic resistance so that the right ventricular systolic pressure is higher than the left If there is an associated ventricular septal defect the ventricular pressures are equalised as in Fallot s tetralogy by a shunt flow from right to left Without such a safety valve right ventricular pressures may rise very high indeed and the right atrial pressure also owing to the resistance of the thick right ventricle to extra diastolic stretch If the foramen ovale is patent or if there is an associated atrial septal defect shunt reversal then takes place at atrial level thereby relieving the right ventricle of some of its load

In cases of mild or moderate severity pressures in the right side of the heart are lower than in the left and an associated ventricular septal defect or atrial septal defect results in the usual direct left to right shunt

## CLINICAL FEATURES

In view of the physiological situation described above it is clear that the clinical behaviour of cases of pulmonary stenosis must vary greatly according to the severity of the lesion In the present series of 170 cases the stenosis was mild in 38 per cent moderate in 25 per cent and severe in 37 per cent These three groups will be discussed first separately

*Mild uncomplicated cases*

There are no symptoms and effort tolerance is normal All cases are acyanotic

The only abnormal physical sign is a loud pulmonary systolic murmur usually initiated by a pulmonary ejection click (Leatham and Vogelpoel 1954) and accompanied by a thrill in 86 per cent There is no significant *a* wave in the venous pulse the cardiac impulse is normal (left ventricular) there is no lift over the right ventricle and the second heart sound is obviously split with the pulmonary element quite loud and clear

The electrocardiogram is normal Skiagrams show characteristic post stenotic dilatation of the pulmonary artery but nothing else abnormal

*Uncomplicated cases of moderate severity*

There are still no symptoms and all cases are acyanotic Effort tolerance is usually normal Included amongst the 80 patients with uncomplicated pulmonary valve or infundibular stenosis of mild or moderate grade were a New Zealand long distance swimming champion a woman athlete a Cambridge University wing three quarter a captain of a regional English hockey XI and a first class long distance runner

In addition to the thrill and murmur the physical signs now include slight exaggeration of the jugular *a* wave (about 3 mm Hg) an impalpable left ventricle and wide splitting of the second heart sound the pulmonary component being late none too loud, curiously brief and rather high pitched even metallic in quality



Fig 8 66—Skiagram of a case of simple pulmonary valve stenosis showing post stenotic dilatation of the pulmonary artery

The electrocardiogram always shows some degree of right ventricular preponderance usually grade 2 sometimes grade 1 or grade 3 but never grade 4 A small P pulmonale (2 mm /0 08 sec ) is seen in about 40 per cent of cases

Fluoroscopy still reveals no more than post stenotic dilatation of the pulmonary artery in one third of the cases (fig 8 66) but in two thirds there is now slight enlargement of the right side of the heart and occasionally (15 per cent) slight pulmonary ischæmia

*Uncomplicated severe cases*

When the stricture is severe *effort dyspnœa* ranges between none (10 per cent) slight (30 per cent) moderate (30 per cent) and considerable or gross (30 per cent together) *Angina pectoris* occurred in 15 per cent of the 32 uncomplicated cases in the present series and *syncope* in 12 per cent

The physical signs are highly characteristic and usually pathognomonic The face is highly coloured unusually full even bloated (moon facies) in one third of the cases not unlike that in patients treated with A C T H (fig 8 67) Cyanosis when present is peripheral unless the foramen ovale is patent (*vide infra*) The pulse is usually small and the blood pressure normal or rather low



Fig 8 67—The moon facies in a case of pulmonary valve stenosis

There was a *giant a wave* (fig 8 68) in the jugular venous pulse reaching 5 to 15 mm Hg above the sternal angle in half the severe cases and a smaller but clearly dominant *a* wave measuring about 3 mm Hg in a quarter Of the remainder some had a normal venous pulse and a similar number had gross tricuspid incompetence The giant *a* wave is of course presystolic in timing peculiarly abrupt and collapsing in quality (like a venous Corrigan s sign) can be felt as well as seen and is transmitted to the liver it leaps to the eye towering above and dwarfing the other waves of the venous pulse (Abrahams and Wood 1951)

The left ventricle is always impalpable in severe cases but a conspicuous *right ventricular heave* may be seen and felt from the left sternal edge to the mid clavicular line or beyond, this parasternal lift should be felt as high as the third space provided the stenosis is valvular

*Right atrial presystolic gallop* usually accompanies the giant *a* wave A pulmonary ejection click does not occur in severe cases (Leatham and Vogelpoel 1954) A loud and long *pulmonary systolic murmur*, invariably accompanied by a thrill spills through the aortic second sound and the *pulmonary second sound* is either inaudible or both very late and very quiet With only two exceptions the murmur was heard best in the second left space in all these cases of valve stenosis

The *electrocardiogram* invariably shows considerable or gross right ventricular preponderance (fig 8 69) apart from rare instances in which

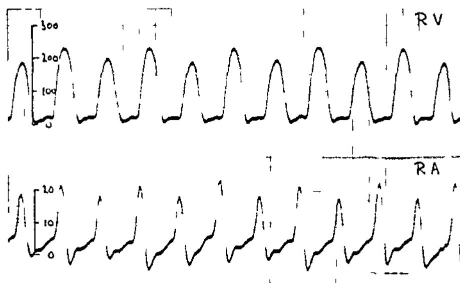



Fig 8 68—Giant *a* wave measuring 20 mm Hg in a case of severe pulmonary valve stenosis note the alternation in both right atrial and ventricular pressures

there is fully developed right bundle branch block A tall P pulmonale averaging 3 mm nearly always accompanies the QRS T changes

*Skiagrams* show a small aorta post stenotic dilatation of the pulmonary artery light pulmonary vascular markings and a variable degree of right atrial and ventricular enlargement (fig 8 70) occasionally the latter is so gross that it masks the dilated pulmonary artery

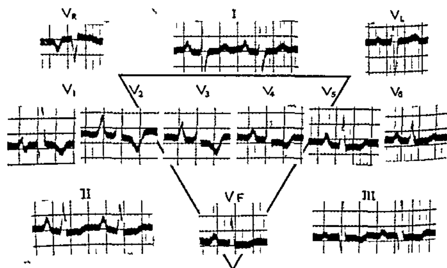



Fig 8 69—Gross right ventricular preponderance in a case of severe pulmonary stenosis (infundibular)




Fig 8 70—Severe pulmonary valve stenosis showing a small aorta conspicuous dilatation of the pulmonary artery pulmonary ischæmia and considerable dilatation of the right side of the heart

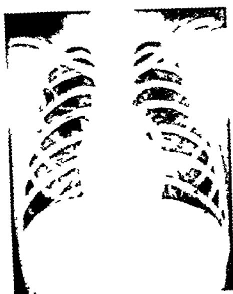


Fig 8 71—Infundibular stenosis showing no dilatation of the pulmonary artery

## *INFUNDIBULAR STENOSIS*

Simple infundibular stenosis whether mild moderate or severe differs from the type described above in three respects only (1) no right ventricular lift may be felt as high as the third left space (2) the thrill and murmur are usually maximum low down in the fourth space or even at the apex (3) there is rarely radiological evidence of post stenotic dilatation of the pulmonary artery (fig 8 71) Unfortunately there are exceptions to all these rules but the first is true in over half the cases the second in 80 per cent and the third in 85 per cent When mild or moderate infundibular stenosis is usually mistaken for maladie de Roger

## *PULMONARY STENOSIS WITH DIRECT SHUNT*

When an atrial or ventricular septal defect complicates pulmonary stenosis with normal aortic root the shunt is direct from left to right if the stricture offers less resistance to flow than the systemic peripheral resistance The clinical features vary according to the degree of stricture and the size of the defect and are determined chiefly by the dominant lesion

When atrial septal defect is dominant pulmonary stenosis should be suspected if there is a pulmonary ejection click a coarse systolic thrill and

unusually wide splitting of the second heart sound When ventricular septal defect is dominant the stenosis is usually overlooked When pulmonary valve or infundibular stenosis is dominant relatively small direct shunts are apt to escape notice but may be suggested by discrepancy between the size of the right ventricle and the pulmonary vascular shadows

## *PULMONARY STENOSIS WITH REVERSED INTERATRIAL OR INTERVENTRICULAR SHUNT*

Moderately severe cases of pulmonary stenosis may have a patent foramen ovale that is functionally closed As life advances, the stricture may tighten the pressure in the right side of the heart then rises and the foramen ovale may suddenly begin to function and permit the passage of blood from right to left atrium Such cases illustrate very well what is meant by late central cyanosis or cyanose tardive. Patients with pulmonary stenosis and A S D or V S D may behave similarly

The change is apt to occur in adolescence and is accompanied by the development of breathlessness (Allanby and Campbell 1949) Cyanosis is notably variable and patients may only turn blue on exertion Pulmonary stenosis with reversed interventricular shunt resembles Fallot s tetralogy, but the aorta is not over riding

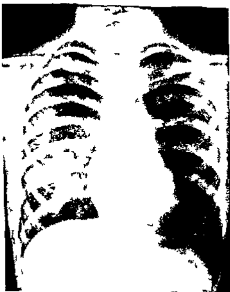
In most severe cases of pulmonary stenosis however the pressure in the right atrium exceeds that in the left from birth and the foramen ovale cannot close Under these circumstances patients have permanent central cyanosis and proportionate functional incapacity from birth In the present series of 30 cases with reversed interatrial shunt breathlessness and cyanosis had been present since birth in 80 per cent cyanosis had appeared first between the ages of 8 and 16 in 12 per cent and the remainder were clinically acyanotic at rest According to Joly *et al* (1950) the condition was described by Fallot in 1888 and has therefore been called Fallot s trilogy by the French school

The clinical features are similar to those of severe pulmonary stenosis with closed septa with the addition of *central cyanosis clubbing* and *polycythæmia*, together with certain other modifications *Effort intolerance* usually dating from birth is moderate or considerable with equal frequency in the vast majority occasionally it is gross (and of course must become so in the end) but it is very rarely slight Since the right ventricle is spared some of the load and therefore fares better than cases of equal severity without a defect in the atrial septum (Brecher and Opdyke 1951) the greater effort intolerance must be due to the drop in arterial oxygen saturation as it is in Fallot s tetralogy Both angina pectoris and syncope occurred only twice each in the 30 cases comprising this series

A *moon facies* was seen in a quarter of the cases *arachnodactyly* in 11 per cent and hypertelorism in two instances A *giant a wave* 5 to 55 mm Hg in amplitude was recorded in 60 per cent and a dominant *a*

3 mm Hg above *v* in 26 per cent Two of the cases with giant *a* waves that came to necropsy had large atrial septal defect , so that powerful right atrial contraction does not necessarily mean a small foramen ovale A *right ventricular heave* was slight (or even absent) in half the cases moderate in a quarter and considerable in a quarter

The characteristic *thrill and long murmur* and their lower position when the stenosis was infundibular were the same as in acyanotic cases The thrill was absent in only two instances The *second heart sound* was single (aortic) in all but three cases and in these it was very late A very soft late P could often be demonstrated however phonocardiographically In three instances a soft relatively short mid diastolic murmur could be heard in the third left space and was attributed to turbulence set up at the atrial septal defect in two others there was a murmur strongly suggesting slight pulmonary incompetence



(a) Showing dilatation of the pulmonary arc and pulmonary ischæmia



(b) Showing considerable cardiac enlargement and pulmonary ischæmia

Fig 8 72—Pulmonary stenosis with reversed interatrial shunt

*Teleradiograms* showed considerable dilatation of the right heart in only a quarter of the cases moderate enlargement being the rule and slight or no enlargement occurring in one third (fig 8 72) There was usually more pulmonary ischæmia than in acyanotic cases Post stenotic dilatation of the pulmonary artery was seen in nearly all those with valve stenosis

The *electrocardiogram* showed evidence of considerable or gross right atrial and right ventricular hypertrophy in 85 per cent

DIFFERENTIAL DIAGNOSIS -

*Mild pulmonary stenosis* may be confused with atrial or ventricular septal defect idiopathic dilatation of the pulmonary artery mild aortic stenosis and normality *Atrial septal defect* should be distinguished by the size and behaviour of the right ventricle the absence of a pulmonary ejection click fixed splitting of the second sound frequent mid diastolic murmur associated with tricuspid turbulence partial right branch block pattern of the electrocardiogram and pulmonary plethora

*Maladie de Roger* is easily confused with mild infundibular stenosis, but may be suggested by the closer splitting of the second heart sound Maladie de Roger should not be mistaken for mild pulmonary valve stenosis in view of the earlier and lower position of the systolic murmur absence of a pulmonary ejection click closer splitting of the second sound and absence of dilatation of the pulmonary artery The clinical features of pulmonary stenosis and ventricular septal defect diverge more and more widely as their severity increases

*Idiopathic dilatation of the pulmonary artery* may give rise to difficulty when the pulmonary ejection click is followed by a grade 2 systolic murmur In fact in such cases it is often impossible to be sure whether there is trivial stenosis or not and one may be still in doubt when cardiac catheterisation reveals a 5 to 10 mm Hg pressure gradient across the pulmonary valve when the right ventricular systolic pressure is still within normal limits

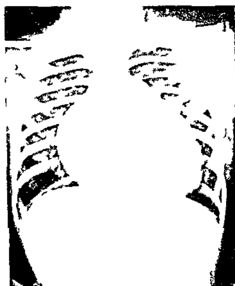


Fig 8 73—Pulmonary valve stenosis with gross dilatation of the right ventricle and atrium resulting in appearances similar to those of Ebstein s disease except for the dilatation of the pulmonary artery

In *mild aortic stenosis* the systolic murmur and thrill begin later and end well before the second heart sound which is closely split $A_2$ being slightly delayed moreover the murmur is well heard at the apex beat and over the right carotid

A *normal heart* with a grade 2 functional pulmonary ejection murmur and prominence of the pulmonary arc radiologically may also be mistaken for mild stenosis

*Pulmonary stenosis of moderate severity* is one of the easiest bedside diagnoses and can hardly be mistaken for anything else whether the stricture is valvular or infundibular

*Severe stenosis* is also unmistakable in acyanotic cases unless there is gross failure In such instances a deep $y$ descent or large systolic wave

from tricuspid incompetence may replace the giant *a* of the jugular pulse the overloaded and grossly distended right heart loses its former vigour and may not be recognised by palpation the electrocardiogram may show right bundle branch block, and X rays reveal a grossly enlarged stencilled heart shadow (fig 8 73) which in view of the findings just mentioned is easily mistaken for that of Ebstein s disease However the typical thrill and murmur of stenosis are still present and the characteristic diastolic scratch of Ebstein s disease is missing moreover it is very rare to meet the full combination of confusing features described above and as a rule a giant *a* wave right ventricular heave high voltage electrocardiogram with gross right ventricular preponderance or post stenotic dilatation of the pulmonary artery makes a diagnosis of Ebstein s disease untenable

*Severe stenosis with reversed shunt* may be confused with *Fallot s tetralogy* Favouring a normal aortic root and atrial septal defect are arachnodactyly a moon facies giant *a* wave considerable right ventricular heave right atrial gallop long systolic murmur and thrill faintly audible late P soft mid diastolic murmur in the third or fourth left space gross right ventricular preponderance electrocardiographically considerable enlargement of the right heart radiologically and post stenotic dilatation of the pulmonary artery for all these features are absent in Fallot's tetralogy

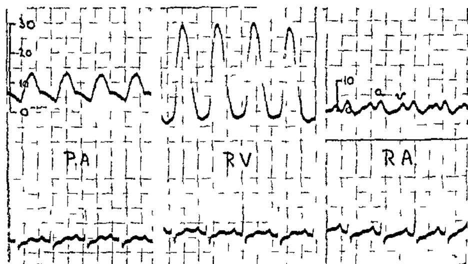
A history of squatting normal venous pressure and pulse quiet heart short systolic thrill and murmur loud single (aortic) second sound moderate right ventricular preponderance electrocardiographically normal transverse diameter of the heart radiologically a poorly defined pulmonary arc and a right sided thoracic aorta all favour Fallot s tetralogy

*PHYSIOLOGICAL FINDINGS* (based on 150 cases catheterised)

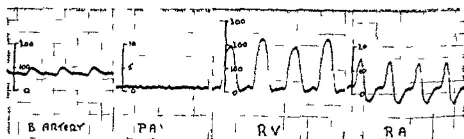
In *mild cases* of pulmonary stenosis with normal aortic root the right atrial pressure is normal the right ventricular pressure 30/0 to 50/0 and the pulmonary artery pressure normal (fig 8 74a) the cardiac output is normal and rises normally with effort with the aid of some elevation in right ventricular pressure The arterial oxygen saturation is normal

In *moderate cases* the findings are similar except that a dominant *a* wave measuring about 3 mm Hg may appear in the right atrial tracing and the right ventricular systolic pressure lies between 50 and 100 mm Hg at rest and may rise well over 100 on effort

In *severe cases* a giant *a* wave rising 5 to 15 mm Hg above the zero point is almost invariable The right ventricular pressure lies between 100/0 and 275/20 at rest the raised end diastolic pressure being usually due to the giant *a* rather than to heart failure The pulmonary artery pressure is usually low (fig 8 74b) The right ventricular systolic pressure is commonly higher than the systemic blood pressure at rest and rises well above it on exercise The cardiac output is low and rises little on exertion the arterio-venous oxygen difference is nearly always over 50 ml per litre and




(a) Mild




(b) Severe

Fig 8 74—Pressure tracings from two cases of pulmonary valve stenosis

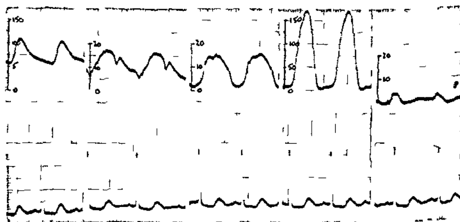


Fig 8 75—Pressure tracings from a case of infundibular stenosis The systolic pressure in the infundibular chamber is the same as that in the pulmonary artery while the diastolic pressure is the same as that in the right ventricle

increases greatly on effort The arterial oxygen saturation is normal in cases with closed septa

*When the stenosis is infundibular* the systolic pressure in the infundibular chamber is the same as that in the pulmonary artery while the diastolic pressure is the same as that in the right ventricle (fig 8 75) The position of the tip of the catheter when the systolic pressure changes provides good evidence concerning the site of the stricture

*Pulmonary stenosis with atrial septal defect or ventricular septal defect* and direct left to right shunt is proved by finding an increased oxygen saturation in samples taken from the right atrium or right ventricle respectively in addition to a significant systolic pressure gradient across the pulmonary valve or infundibulum

*In severe pulmonary stenosis with reversed interatrial shunt* it is usually possible to pass the catheter through the defect into the left atrium and left ventricle or out into a pulmonary vein (fig 8 76) In the 30 cases catheterised the right ventricular systolic pressure ranged between 105 and 260 averaging 165 mm Hg and was usually well above the left ventricular pressure (fig 8 77) Giant *a* waves in right atrial pressure tracings were never transmitted to the left atrium in cases with relatively small shunts due to patent foramen ovale (fig 8 77) but were seen occasionally in left atrial tracings when the shunt was large and due to atrial septal defect proper The arterial oxygen saturation averaged 75 per cent and arterial samples were similar to those obtained from the left ventricle but left atrial samples varied considerably according to whether the tip of the catheter was lying in the shunt stream or near the mouth of a pulmonary vein Pulmonary venous samples were always normally saturated

In the differential diagnosis between pulmonary stenosis with reversed interatrial shunt and Fallot s tetralogy there are two points of crucial importance (1) a catheter may pass through a valve patent foramen ovale in Fallot s tetralogy but when it does so left atrial samples are usually fully saturated the foramen being functionless (2) when the right ventricular systolic pressure is more or less the same as the systemic blood pressure simultaneous or immediately consecutive right ventricular and brachial arterial pressures should be recorded both at rest and on exercise for in Fallot s tetralogy they remain identical whereas in pulmonary stenosis with reversed interatrial shunt they do not Slight differences between right ventricular and systemic arterial pressures at rest may be due to artefact or over damping in one of the systems or to a slight local build up of pressure in the femoral artery if that vessel is used and do not therefore exclude Fallot s tetralogy

*Selective dye concentration curves* may prove the site of a reversed shunt If Evans blue dye is injected into the right ventricle for example it appears immediately in the ear only when the shunt is at ventricular or aorto pulmonary level



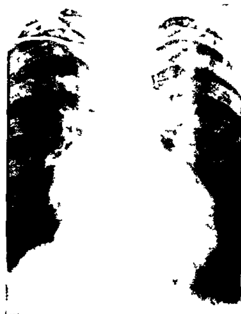
(a)



(b)



(c)



(d)

Fig 8 76—Pulmonary stenosis with reversed interatrial shunt the catheter has passed through the defect and is lying (a) in the right upper pulmonary vein (b) in the right lower pulmonary vein (c) in the left upper pulmonary vein and (d) in the left atrium close to the mitral valve

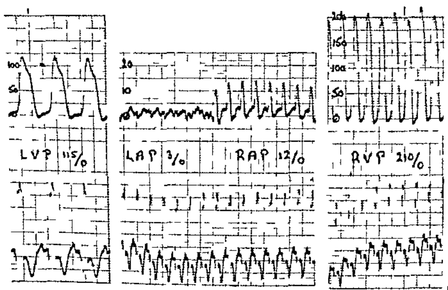



Fig 8 77—Pressure tracings from a case of pulmonary valve stenosis with reversed interatrial shunt showing giant *a* waves in the right atrium but not in the left

## *ANGIOCARDIOGRAM*

Routine intravenous angiocardiograms demonstrate the site of pulmonary stenosis in the majority of cases but by no means in all selective angiocardiograms obtained after injecting diaginol into the right ventricle preferably through a wide catheter provided with lateral holes near the tip so as to avoid recoil are more informative (Jonsson Broden and Karnell 1953) Whether the stricture can be seen directly or not angiocardiography may confirm the diagnosis of pulmonary stenosis in three indirect ways (1) there is a hold up in the passage of the contrast medium through the right side of the heart which is proportional to the severity of the stricture (2) during systole in cases of valve stenosis powerful contraction



Fig 8 78—Angiocardiogram in a case of pulmonary stenosis with reversed intra atrial shunt the contrast medium is passing through both sides of the heart simultaneously

of the hypertrophied infundibulum may cause remarkable narrowing of the outflow tract (3) post stenotic dilatation of the pulmonary artery is well demonstrated in cases of valve stenosis

In cases with reversed interatrial shunt there is more or less simultaneous filling of both sides of the heart (fig 8 78) With selective angiocardiography simultaneous filling of the aorta and pulmonary artery is only seen when diaginol is injected into the right atrium

## *COURSE AND PROGNOSIS*

The average age of death in cases that have come to necropsy was 20 6 years in Abbott s (1931) series 22 8 years in the group reported by Bauer and Astbury (1944) and 26 in the series reviewed by Green *et al* (1949) The usual cause of death was congestive heart failure which was three times as common as bacterial endocarditis It follows that these serious mortality figures apply chiefly to severe cases for mild stenosis does not cause heart failure and moderate stenosis is unlikely to do so

The oldest case in Green s series was 75 years the oldest in my own 67 This was a man still in fairly good health apart from emphysema the clinical features fulfilled the criteria for mild or moderate stenosis partly masked by emphysema his right ventricular pressure was 75/3 pulmonary artery pressure 15/3 and right atrial pressure 3 —3 0 —3 for *a x v* and *y* respectively, the cardiac output at the time being 3 7 litres per minute the right ventricle was not dilated radiologically and there were no signs of impending break down There can be little doubt therefore that the prognosis of mild and moderate cases is good apart from the risk of bacterial endocarditis

Severe cases whether acyanotic or with reversed shunt, become progressively incapacitated but may linger on with chronic congestive failure and ascites The oldest acyanotic case in this group was 33 when he died the oldest with central cyanosis 26 years

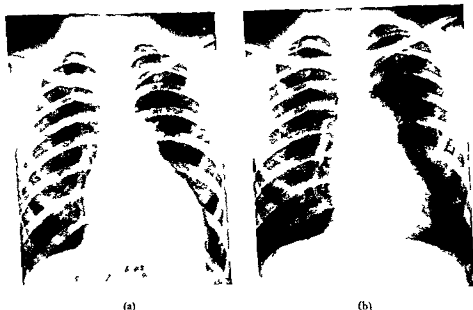
*Bacterial endocarditis* has not yet been witnessed in any case in the present series but two of the patients gave a convincing history of it Prior to the infection both had had grade 3 effort intolerance one of them having had considerable central cyanosis obviously due to reversed interatrial shunt Following cure of the infection both improved remarkably, one being now symptom free the other having only slight effort intolerance These are the only two cases in the whole series with obvious pulmonary diastolic murmurs and it seems reasonable to conclude that the infection performed a medical valvotomy

*Pulmonary tuberculosis* complicated two severe cases one of them acyanotic the other with reversed shunt it was met in only one other instance in this series despite the fact that one of the clinics at which patients were seen was at the Brompton hospital This gives an incidence of about 2 per cent which is the same as in the general population

*TREATMENT*

Mild cases should be encouraged to lead a normal life without any restrictions Cases of moderate severity do not require surgical help and should also be allowed to lead normal lives although competitive effort is probably best avoided Patients in all groups should be protected against dental and other sources of infection by means of penicillin or other suitable antibiotics when the occasion arises

Pulmonary valvotomy (Brock 1948 Brock and Campbell 1950) should be undertaken in all severe cases, preferably around the age of 6 to 10 Infundibular resection is better performed under direct vision either with



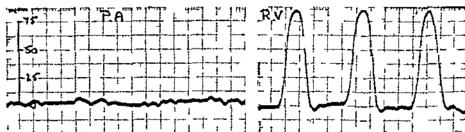
(a) (b)

Fig 8 79—Case of pulmonary valve stenosis (a) before and (b) after valvotomy showing considerable reduction in heart size following the operation

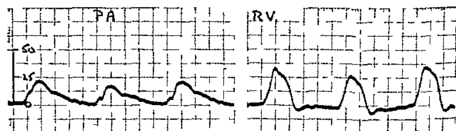
the help of hypothermia or crossed circulation Anastomotic operations are contraindicated in cyanotic cases because the increased pulmonary blood flow that results raises the left atrial pressure and by reducing the reversed shunt increases the load on the right ventricle which frequently fails Secondary elevation of the right atrial pressure then restores the right to left interatrial shunt so that little is gained at considerable cost

Pulmonary valvotomy was undertaken by Sir Russell Brock in 30 patients in this series and infundibular resection in four others The results were excellent or good in a little over half and fair or poor in a quarter 20 per cent died When the result was excellent patients became symptom free and cases with previously reversed shunt lost all trace of

cyanosis and clubbing The right ventricle and atrium diminished considerably in size (fig 8 79) and the electrocardiogram showed less right ventricular preponderance At operation effective valvotomy was considered to have been achieved when the pulmonary artery pressure rose to normal and developed a good pulse pressure while the right ventricular systolic pressure fell to 50 mm Hg or less (fig 8 80)




(a)




(b)

Fig 8 80—Case of severe pulmonary valve stenosis showing pulmonary artery and right ventricular pressure pulse (a) before and (b) after pulmonary valvotomy

At the present time the operative mortality is nearer 6 than 20 per cent (Campbell and Brock 1955) and the results from infundibular resection under direct vision are as good as those for valvotomy apart from the added risk of hypothermia

Pulmonary incompetence has never caused trouble in this group although a faint or moderate pulmonary diastolic murmur has been heard following valvotomy in nearly half the cases

Subsequent cardiac catheterisation a year or two later in a limited number of these cases has revealed physiological findings in harmony with the clinical situation the right ventricular systolic pressure being under 50 mm Hg at rest and the pulmonary artery pressure pulse normal in the best of them

## PULMONARY STENOSIS WITH DEXTROPOSED AORTIC ROOT

## (FALLOT S TETRALOGY)

The combination of pulmonary stenosis patent interventricular septum riding' aorta and enlargement of the right ventricle is known as Fallot s tetralogy (Fallot 1888) and accounts for 66 per cent of cases of congenital heart disease with clubbing of the fingers, polycythæmia and permanent central cyanosis The stenosis is purely infundibular in just over half the cases purely valvular in about a third and both infundibular and valvular in the remainder *The defect in the ventricular septum measures* 10 to 16 mm in diameter according to the size of the heart (Brinton and Campbell 1953) The pulmonary artery instead of being dilated as in simple pulmonary stenosis is remarkably small at least in cases with infundibular stenosis and may resemble a vein By riding aorta is meant displacement of the root of the aorta to the right (dextroposed aorta) so that it sits astride the septum and appears to arise as much from the right as from the left ventricle The association of these three malformations is no accident but depends upon the same embryological defect the fault lying with arrested evolution of the bulbus cordis with incomplete torsion. A right sided aortic arch is found in 20 to 25 per cent of cases (Taussig 1947) an association not found in cases with *normal aortic root* It occurred in 20 per cent of the present series of 100 cases A left sided superior vena cava (always with a right S V C as well) was demonstrated by means of cardiac catheterisation or angiocardiography in 20 per cent also conversely Fallot s tetralogy was present in just over 50 per cent of all cases in which a left S V C was recognised no other condition except perhaps Eisenmenger s complex proper having any special association with it

*Hæmodynamics* Aortic blood is arterio venous being composed of the full output of the left ventricle and part of that from the right The right ventricle competes with the left ventricle against the systemic peripheral resistance, which is less than that of the stricture The situation is met by hypertrophy of the right ventricle, *the fourth constant* finding in the tetralogy The deficient pulmonary circulation is occasionally improved by extensive development of the bronchial vascular system Polycythæmia helps to compensate for anoxæmia

The pressures in the left and right ventricle are always identical and on effort the right ventricular systolic pressure cannot rise above aortic level The right ventricle accommodates itself to this situation from birth and is as thick or thicker than its fellow it is not distended and rarely fails for it can empty freely and quickly into the aorta if the obstruction increases Since left and right atrial pressures are also practically identical in Fallot s tetralogy (easily demonstrated when there is a patent foramen ovale) diastolic ventricular tone must also be much the same on the two

sides This explains why there is no detectable interatrial shunt when there is a patent foramen ovale or small atrial septal defect

Relatively mild cases occur in which the resistance of the stenosis is about the same as the systemic peripheral resistance there is then a bidirectional shunt as in Eisenmenger s complex, or there may be a perfectly balanced state between the two circulations with no detectable shunt either way such cases being acyanotic at rest If the stenosis is milder still a unidirectional left to right shunt can occur as it may also after successful valvotomy or infundibular resection About 10 per cent of all cases of Fallot s tetralogy behave in one of these ways and help to prove that the direction and magnitude of the shunt are determined a great deal more by the total resistances in the two circulations than by the degree of over ride

## FREQUENCY AGE AND SEX

Fallot s tetralogy accounted for 11 per cent of the author s series of 900 cases of congenital heart disease The number per cent in each decade was as follows

| Age group | 0–10 | 11–20 | 21–30 | 31–40 | 41–50 |
|---|---|---|---|---|---|
| No per cent | 50 | 33 | 15 | 1 | 1 |

The average age was 12 years the oldest 42 The sex ratio was 7 4 in favour of males This contrasted with the 3 4 M F ratio in pulmonary stenosis with reversed interatrial shunt

## CLINICAL FEATURES

*Cyanosis polycythæmia* and *clubbing* of the fingers may be absent in infants but develop in early childhood and tend to be progressive Central cyanosis means an arterial oxygen saturation below 85 per cent. Of the 100 cases in this series 15 per cent were acyanotic at rest as described by Wood Magidson and Wilson (1954) and had neither polycythæmia nor clubbing The arterial oxygen saturation ranged between 87 and 97 per cent in this group Polycythæmia was demonstrated in 82 per cent of cyanosed cases Growth may be stunted but mental development is usually normal The bloated facies of severe pulmonary stenosis with normal aortic root is not seen in the tetralogy The chief symptom is *breathlessness* and to obtain maximum comfort children often adopt a characteristic *squatting* posture (Taussig 1947) Squatting improves the arterial oxygen saturation (Lequime Callebaut and Denolin 1950) but the reason for this is not yet clear Effort intolerance is usually considerable (grade 3) and is rarely less than grade 2B even in acyanotic ca es It is attributed to a fall in arterial oxygen saturation on effort and perhaps to some disturbance of ventilation not yet fully understood it is not due to right ventricular strain and temporary overloading of that chamber for nothing of that sort occurs

Angina pectoris is extremely rare but *syncope* occurs in 20 per cent of cases especially in infancy and early childhood Attacks may be related to effort crying breath holding or some other transient disturbance but are often capricious and unexpected Theoretically anoxic syncope might be expected to result from any agent which lowered the systemic resistance sufficiently to cause a critical increase of right to left shunt as demonstrated by Hamilton Winslow and Hamilton (1950) in fact however the blood pressure has not fallen in any of four cases studied by the author, nor did a powerful pressor agent which raised the blood pressure from 100 to 150 mm Hg in an infant make any difference to the grossly reduced pulmonary blood flow It is suggested that syncope in Fallot s tetralogy which is always associated with gross cyanosis and virtual cessation of the pulmonary blood flow, is due either to pulmonary vasoconstriction or to overactivity of the hypertrophied infundibulum so that during systole it blocks the circulation to the lungs Such behaviour on the part of the infundibulum would be no more than an exaggeration of its function in reptiles and amphibia in which it serves as a muscular valve to protect the lungs from the full force of ventricular systole its late systolic contraction deflecting blood from the common ventricle into the systemic aorta (Keith 1924) Functional infundibular stenosis has been demonstrated by means of angiocardiography in cases of Fallot's tetralogy (Hilario Lind and Wegelius 1954) and has been observed by Brock when operating on cases with valve stenosis Pulmonary artery pressure pulses that show a late systolic trough are also highly suggestive

*Physical signs*

The *pulse* and *venous pressure* are usually normal but a small dominant *a* wave rising some 3 cm above *v* is seen in 20 per cent of cases giant *a* waves do not occur

The left ventricle is nearly always impalpable at the expected position of the apex beat and there is very little or no demonstrable lift over the right ventricle in 90 per cent of cases, a moderate lift occurring in the remainder A strong grade 3 right ventricular heave practically excludes Fallot s tetralogy Pulsation can never be felt in the second space over the pulmonary artery

There is always a *systolic murmur* over the outflow tract of the right ventricle maximum as a rule in the third left space but occasionally higher or lower It is loud in 85 per cent moderate in 12 per cent and soft in 3 per cent A *thrill* accompanies 85 per cent of the loud murmurs but not the others it is therefore present in nearly three quarters of all cases The murmur is caused by turbulence set up at the stricture and is not due to the shunt It is a pulmonary or infundibular ejection murmur, starting early because the pulmonary diastolic pressure is low and finishing usually just before the aortic second sound it does not spill through $A_2$ like the long murmur of severe pulmonary stenosis with normal aortic root

(Vogelpoel and Shrire 1955) This may be because the right ventricle empties relatively quickly as previously described or because of total (partly functional) infundibular obstruction in late systole As might be expected the intensity and length of the murmur vary inversely with the pulmonary blood flow, and diminish greatly during spontaneous attacks of increased cyanosis with syncope the murmur usually disappears altogether (functional pulmonary atresia) Conversely after pulmonary valvotomy or infundibular resection the murmur often becomes explosive

The *second heart sound* is invariably single and usually fairly loud at the base because the root of the aorta is uncovered and it is only aortic valve closure that is heard There is no gallop no ejection click no pulmonary diastolic murmur and no mid diastolic murmur I have yet to hear a continuous murmur in Fallot's tetralogy whether due to patent ductus which must be extremely rare or to a broncho pulmonary communication Indeed such a murmur occurring in a case which has many features suggesting Fallot s tetralogy makes a diagnosis of pulmonary atresia virtually certain

*Electrocardiogram*

The P pulmonale is often said to be typical of Fallot s tetralogy and has been reported as occurring in 80 per cent of cases (Donzelot *et al* 1951) This statement needs tempering for it is near the margin of truth and is physiologically misleading The right ventricle is not ordinarily embarrassed in Fallot s tetralogy and needs relatively little atrial help in the 100 cases analysed here the P wave was normal in 42 per cent 2 to 2 5 mm high in the most favourable lead in 26 per cent 3 to 3 5 mm high in 25 per cent and 4 or more mm high in 7 per cent Thus in two thirds of the cases it did not exceed 2 5 mm While it is agreed therefore that a P pulmonale is common in Fallot s tetralogy its small stature and the frequency of a normal P wave are stressed for in these respects the P wave differs from its behaviour in pulmonary stenosis with reversed interatrial shunt

Right ventricular preponderance as customarily interpreted from multiple chest leads was slight in 9 per cent of cases moderate in 24 per cent considerable in 57 per cent and gross in 7 per cent the graph being normal in 3 per cent Here again the point that requires emphasis is the relatively minor change found in one third of all cases (fig 8 81) in remarkable (but expected) contrast to the findings in severe pulmonary stenosis with normal aortic root There was no convincing correlation between the grade of right ventricular preponderance and the degree of cyanosis or effort intolerance for example when right ventricular preponderance was slight or moderate one third of the cases had considerable or gross cyanosis when it was grade 3 or 4 41 per cent had considerable or gross cyanosis This is not surprising because the work of the right ventricle is the same whether cyanosis is absent or gross and whether the

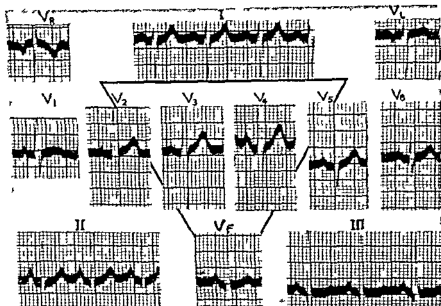



Fig 881—Electrocardiogram in a typical case of Fallot's tetralogy showing a small P pulmonale in lead 2 and only slight right ventricular preponderance

stenosis is relatively mild or extreme for it is determined by its stroke volume and the systemic peripheral vascular resistance If in fact there is some relationship between the degree of right ventricular preponderance and the size of the shunt it could only be explained by a difference in left ventricular work with a large shunt and small pulmonary blood flow the left ventricle is underfilled and therefore performs less work with little or no shunt and a relatively good pulmonary blood flow it is well filled and therefore performs more work On the whole the findings best fit the thesis (based on direct surface leads at operation) that in Fallot's tetralogy the electrocardiographic appearances at any rate in respect of QRS are due to strong clockwise rotation of the heart so that the tall R wave of lead $V_1$ is really left ventricular (McGregor 1950)

*X ray*

The skiagram is usually pathognomonic under the clinical circumstances and is characterised by conspicuously clear lung fields due to diminution of the pulmonary blood flow by a notable gap between the aortic knuckle and ventricles due to hypoplasia of the pulmonary artery and by a tip tilted cardiac apex (fig 882) This is the cœur en sabot for it resembles the shape of a peasant's wooden shoe with turned up toe The effect is produced by considerable hypertrophy of the right ventricle with displacement of the interventricular septum to the left so that the left ventricle appears as a small cap above the right ventricular apex Occasionally the lung fields present a reticular appearance representing





(a) Anterior view (b) Second oblique position

Fig 8 82—Skiagram of a case of Fallot s tetralogy showing the cœur en sabot

development of the bronchial circulation The transverse diameter of the heart is usually normal in the anterior view In the left anterior oblique view the heart shadow may be globular owing to the increased curvature of the right atrium and ventricle If the aorta is right sided the knuckle may be seen above the right atrium (fig 8 83) and the barium filled œsophagus is deflected to the patient s left In the present series a radiological diagnosis could be made with confidence under the clinical circumstances in 70 per cent of cases pulmonary ischæmia was present in all of these a bay in the region of the pulmonary artery in 70 per cent of them (half the whole series) and a sabot shaped apex in 64 per cent of them (45 per cent of the whole series) A right sided thoracic aorta was present in 20 per cent On the other hand the appearances were strictly normal in 15 per cent (fig 8 84) and the pulmonary artery was slightly dilated in 8 5 per cent (fig 8 85) The rest were atypical



Fig 8 83—Right sided aortic arch and dorsal aorta in a case of Fallot s tetralogy

The shunt may be demonstrated by means of angiocardiography



Fig 8 84—Virtually normal sk agram in a case of acyanotic Fallot s tetralogy

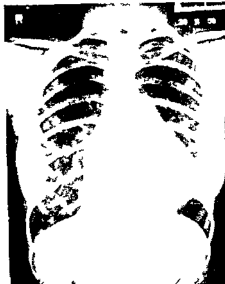


Fig 8 85—Skiagram sho ing dilatat on of the pulmonary artery a sabot shaped apex more enlargement of the right heart than usual and a very prominent inferior vena cava in a proved case of Fallot s tetralogy

I g 8 86—Angiocard ogram of a case of Fallot s tetralogy showing imultaneous opac fi cat on of th aorta and pulmonary artery The tenosis appe r to be infundibul Both pulmonary and both sub lavian art can b seen

(Grishman Steinberg and Sussman 1941) which shows immediate filling of the aorta and great vessels from the right ventricle and undersized pulmonary arteries (fig 8 86) The antero posterior view is advised in order to reveal the anatomy of both subclavian arteries—a point of interest to the surgeon using Blalock s technique

The stenosis itself is rarely seen (Lowe 1953) unless the technique is exceptionally good or selective angiocardiography is employed The medium passes through the heart quickly in Fallot s tetralogy there being no delay in the right ventricle as in pulmonary stenosis with closed ventricular septum and the pulmonary arteries themselves are always densely opacified

## *PHYSIOLOGICAL FINDINGS*

Of 84 cases catheterised the pulmonary artery was entered in 85 per cent the aorta in 27 per cent the left atrium in 17 per cent and the left ventricle in 6 per cent When the pulmonary artery could not be reached the aorta was entered as often as not (6 out of 12 such cases) failing that it was at least possible to take immediately consecutive pressure tracings from the right ventricle and brachial or femoral artery The following observations are based on this experience

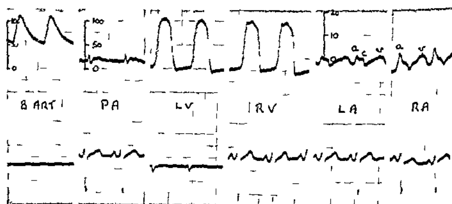



Fig 8 87—Intracardiac pressure tracing from a case of Fallot s tetralogy showing virtually identical systolic pressures in the brachial artery left ventricle and right ventricle

The characteristic findings include a low pulmonary artery pressure with a poor often deformed pressure pulse averaging 9/2 mm Hg (mean 5) above the sternal angle a right ventricular systolic pressure identical with the aortic or brachial systolic pressure under all circumstances identical or nearly identical pressures in both atria and both ventricles respectively and an *a* wave in the right atrial pressure pulse averaging only 2 to 2 5 mm Hg above o and never exceeding 5 mm Hg (fig 8 87) the arterial oxygen saturation ranged between 43 and 87 per cent in cyanotic cases (average 73 per cent) and between 86 and 97 per cent in acyanotic cases (average

91 4 per cent) Left atrial samples were invariably between 90 and 97 per cent saturated and averaged 93 4 per cent proving the absence of reversed interatrial shunt despite the patent foramen ovale Left ventricular samples ranged between 74 and 92 per cent saturated averaging 81 per cent in these cases the arterial oxygen saturation averaged 78 per cent proving that the shunt in Fallot s tetralogy is chiefly at ventricular level as it is in Eisenmenger s complex and not a matter of the right ventricle expelling part of its contents directly into an over riding aorta it is unlikely that any appreciable shunt takes place in diastole for if diastolic ventricular pressures favoured a right to left shunt at ventricular level they must also do so at atrial level which has already been proved untrue Bidirectional shunt was never found in cyanotic cases and only once in the acyanotic group but in three of the latter no shunt at all could be demonstrated and in one there was a unidirectional slight left to right shunt

The site of the stenosis can be recognised as high intermediate or low during cardiac catheterisation but while the last two denote infundibular stenosis it is impossible to be sure whether a high site means valve stenosis or high infundibular stenosis It is most unusual in Fallot s tetralogy to be able to reproduce the clean type of infundibular tracing obtained in the great majority of cases of infundibular stenosis with normal aortic root

In calculating the size of the shunt the pulmonary blood flow must be worked out on the assumption that pulmonary venous blood is 95 per cent saturated In the present series the systemic blood flow averaged 5 L/min and the pulmonary flow 3 L /min giving an average shunt of 2 L /min

*Dye Concentration Curves*

Evans blue dye reaches the ear well ahead of normal time as its rapidly built up concentration levels out or falls off it is suddenly reinforced by dye that has circulated through the lungs If the dye is injected directly into the right ventricle its immediate appearance in the ear proves that the reversed shunt is at ventricular or aorto pulmonary level not below

If an oximeter is not available saccharin or some other test substance may be injected into the right ventricle with similar qualitative results

## *DIFFERENTIAL DIAGNOSIS*

The chief difficulty is to distinguish Fallot s tetralogy from *pulmonary stenosis with reversed interatrial shunt* In their characteristic form these two conditions are very different but when atypical may be remarkably similar (see page 417)

*Pulmonary atresia* is easily recognised by the absence of a pulmonary ejection murmur the almost invariable presence of a continuous murmur under one or other or both clavicles and the more conspicuous ascending aorta

*Eisenmenger s complex* proper with a single second heart sound and

minimal dilatation of the pulmonary artery may cause real difficulty Absence of squatting slight pulsation over the pulmonary artery, a pulmonary ejection click absence of a pulmonary systolic thrill the presence of a Roger murmur and a faint pulmonary diastolic murmur are all strongly in favour of pulmonary hypertension with reversed interventricular shunt

Acyanotic examples of Fallot s tetralogy are usually confused with *maladie de Roger* The history alone should prevent any such error for effort intolerance is at least moderate in the former and invariably absent in the latter The chief differences in the physical signs are the timing of the murmur and the character of the second heart sound the murmur is a pulmonary ejection murmur in Fallot s tetralogy a pansystolic shunt murmur in maladie de Roger the second heart sound is always single in Fallot s tetralogy split in maladie de Roger

## COMPLICATIONS

*Pulmonary tuberculosis* complicated only 2 per cent of the cases in this series which is similar to its incidence in the general population

*Cerebral abscess* presumably from a small paradoxical embolism is responsible for death in about 5 per cent of all fatal cases of congenital heart disease (Robbins 1945 Gates Rogers and Edwards 1947) Fallot s tetralogy has been the primary lesion in half the reported cases The abscess which is usually solitary is not secondary to bacterial endocarditis but to some somatic infection often of a trivial nature A history of such infection however has been obtained in only a third of the cases (Sancetta and Zimmerman 1950)

*Cerebral thrombosis* with hemiplegia is not uncommon especially in infancy and is attributed to polycythæmia

*Bacterial endocarditis* is relatively uncommon probably because of the high natural mortality of most cyanotic forms of congenital heart disease in childhood and adolescence

## PROGNOSIS

Uncomplicated relatively mild cases may reach middle life but the majority die young According to Campbell (1948 1950) only one patient in ten with congenital cyanotic heart disease reaches the age of 21 only one in five reaches puberty and only one in two reaches the age of 7 The most common cause of death in infancy and early childhood is undoubtedly *syncope* the mechanism of which has already been discussed *Bacterial endocarditis* and *cerebral abscess* each takes its toll of about 10 per cent and *cerebral thrombosis* may be fatal *Intercurrent infection* is probably responsible for most of the remainder not because these children are especially prone to such infections but because they tolerate them badly *Congestive heart failure* is very unusual, for as stated repeatedly the right ventricle

is not overburdened in Fallot s tetralogy According to Rich (1948) 90 per cent of fatal cases show widespread thrombotic obstruction of the small pulmonary vessels possibly due to polycythæmia Just what part this plays is open to question an increased pulmonary vascular resistance has yet to be demonstrated at catheterisation

## *TREATMENT*

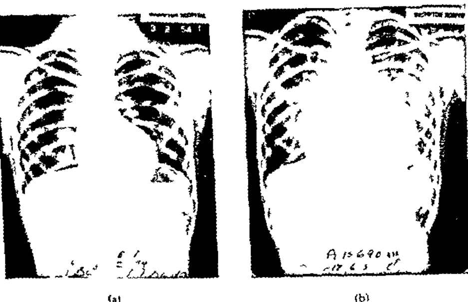
Since the operative mortality is around 30 per cent in infants under 3 years old it is wise to defer operation until the child is 5 or 6 if possible In severe cases the wait may be trying and not without its own mortality Attacks of severe dyspnœa and cyanosis with or without syncope are the chief danger For these Taussig (1948) advised placing the child in the knee chest position and if relief was not immediate giving morphine in a dose of 1 mg per kilogram of body weight which she found almost specific An oxygen tent may have to be used in the worst cases to carry the infant through a difficult period This usually increases the arterial oxygen by about 10 per cent as noted by Taussig and Blalock (1947) when oxygen was given by the anæsthetist as a preliminary to opening the thorax Operation should not be delayed after the age of 3 however if serious attacks continue

As a result of Taussig s observation that infants with Fallot s tetralogy deteriorated when the ductus arteriosus closed and that cases complicated by persistent patent ductus fared better than those without she and Blalock devised the anastomotic operation that proved so successful (Blalock and Taussig 1945 Blalock 1946 1947) One or other subclavian artery is anastomosed to the homolateral branch of the pulmonary artery. Better alignment is obtained as a rule with the right subclavian but the left has a longer intrathoracic course and is therefore easier to bring down If results are poor a second anastomosis may be carried out later on the opposite side Another method of achieving the same object is to make a direct anastomosis between the aortic arch and the left pulmonary artery (Potts *et al* 1946 1948)

The physiological results of technically successful anastomosis are good cyanosis and clubbing may disappear breathlessness decreases the habit of squatting is usually given up and effort tolerance improves the arterial oxygen saturation rises to the region of 80 per cent and the blood count returns to normal (Taussig 1948) a loud machinery murmur and coarse thrill may be detected on the homolateral side immediately after the operation in nearly all cases and are permanent Blalock s total mortality rate for this operation is 17 per cent but this includes infants (mortality rate 25 per cent) cases of tricuspid atresia and other anomalies His mortality rate for selected cases of Fallot s tetralogy is not more than 10 per cent The results and mortality rate of Potts operation are much the same (Potts 1949)

Both Brock (1948) and Sellors (1948) however, proved that pulmonary stenosis was amenable to direct attack the approach being through the wall of the right ventricle Valvotomy is undertaken when the stenosis is valvular infundibular resection (Brock 1949) when the stricture is below the valve Campbell Deuchar and Brock (1954) have reported the results on the first 100 cases of Fallot s tetralogy treated by valvotomy (37 cases) infundibular resection (45 cases) or both (18 cases) at Guy s Hospital and the Brompton Hospital Two thirds of them were greatly improved one sixth were better but not in the same class and nearly one sixth died as a result of the operation the mortality from pulmonary valvotomy was stated to be 11 per cent and from infundibular resection 18 per cent Although the risk was greater with infundibular resection the results were better in those who survived Campbell and Deuchar (1953) also report the results of 200 Blalock Taussig anastomotic operations most of which were undertaken for Fallot s tetralogy A comparison of the results obtained in the two types of operation by the same team is especially valuable The mortality in the anastomotic operation in Fallot s tetralogy was only 8 per cent and 75 per cent of the cases ' benefited greatly but the authors were careful to say that some incapacity usually remained and that cyanosis clubbing and polycythæmia were not as a rule abolished though much reduced The matter may be summed up by saying that the reports from Guy s indicate that the best immediate results are obtained by infundibular resection at the cost of twice the operative mortality The physiological results from pulmonary valvotomy were not quite so good but probably better than from the Blalock Taussig operation on the other and the operative mortality was a little higher

Personal experience at Brompton and elsewhere has been more or less similar but enthusiasm for the Blalock Taussig operation is difficult to maintain These patients are better than they were but none of them can be classed as excellent most of them are still somewhat cyanosed and a little clubbed and effort tolerance is still limited At the Brompton Hospital 41 direct operations have been carried out on cases of Fallot s tetralogy mostly by Sir Russell Brock There were 15 primary pulmonary valvotomies and 26 primary infundibular resections seven cases had the combined operation There were only two deaths in this series, one from valvotomy the other from infundibular resection There is no doubt at all that when the operation was technically satisfactory the results if judged by effort tolerance and disappearance of cyanosis far exceeded anything seen following Blalock s operation Excellent results of this kind were observed in at least 40 per cent more often from infundibular resection than from pulmonary valvotomy as in the Guy s group But half the excellent cases produced by infundibular resection have been transformed into cases of ventricular septal defect with left to right shunt the pulmonary resistance remaining normal The shunt is quite considerable there is radiological pulmonary plethora and the hearts are much enlarged



(a) (b)

Fig 8 89—Skiagrams (a) before and (b) after infundibular resection in a case of Fallot's tetralogy showing post operative pulmonary plethora and considerable enlargement of both sides of the heart

(fig 8 88) Physiological studies in four members of this group a year or two after the operation revealed a pulmonary blood flow of 6 3 to 10 6 litres per minute (average 8 4) which was about twice the systemic flow In three of them the shunt was purely from left to right despite the over riding aorta in the fourth it may have been bidirectional for the arterial oxygen saturation was 88 per cent Right ventricular systolic pressures remained identical with those in the aorta or brachial artery the systolic pressures in the infundibular chamber and pulmonary artery were normal in two cases and raised in the other two (fig 8 89) Nothing approaching Eisenmenger's complex was ever seen The enlargement seems to be due to dilatation of both ventricles particularly the right resulting from their increased stroke volume and is greater than in simple ventricular septal defect with comparable shunt This is because the right ventricle has to pump double its normal volume at systemic pressure an uncommon physiological situation In simple ventricular septal defect with 2 1 shunt the pulmonary artery pressure is usually normal in Eisenmenger's complex when the right ventricle is working at systemic pressure its stroke volume is usually normal

In the other half of the group with excellent results following infundibular resection and in all excellent results following valvotomy the physiological situation is well nigh as perfect as it can be in the presence of a large ventricular septal defect and an over riding aorta for the two circulations appear to be delicately balanced Effort tolerance is practically

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normal there is no cyanosis clubbing or polycythæmia the arterial oxygen saturation is around 90 per cent the heart is only slightly if at all larger and the pulmonary vascular shadows have improved without becoming plethoric (fig 8 90)

At operation one of the technical difficulties is to know when sufficient infundibular resection has been achieved The ideal physiological result is to restore the arterial oxygen saturation to normal without increasing the pulmonary blood flow beyond normal or at most beyond a critical safe limit (probably about 6 litres per minute at rest for a child of 10) Under the artificial conditions imposed by anæsthesia oxygen administration thoracotomy and cardiotomy much experience and fine judgment are necessary if the surgeon is to achieve this ideal he cannot rely on the

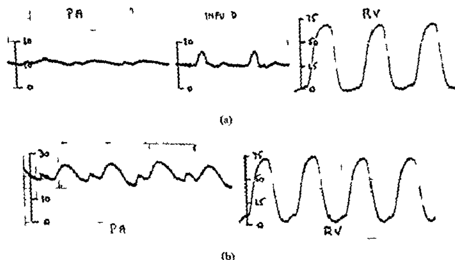



Fig 8 91—Intracardiac pressure pulse (a) before and (b) after infundibular resection in a case of Fallot s tetralogy in (b) the pressure pulse in the pulmonary artery is much better defined and at a higher level the right ventricular systolic pressure is unchanged

oximeter and can obtain no help from the right ventricular pressure which remains at systemic level under all circumstances he can however aim at producing a good pressure pulse in the pulmonary artery without an abnormal rise in pressure (fig 8 91)

There is not the same risk of over zealous surgery when undertaking pulmonary valvotomy So far there have been no examples of serious cardiac enlargement resulting from too great a shunt in this group on the contrary the difficulty has been to achieve a sufficiently good valvotomy to prevent the right to left shunt and to ensure a good pulmonary blood flow A determined attempt to split the valve efficiently however carries with it a risk of another sort that of causing serious pulmonary incompetence A pulmonary diastolic murmur has developed in one quarter of

these cases following valvotomy and in three instances the leak was by no means trivial in fact one is very serious and has led to heart failure Pulmonary incompetence is rarely important unless a left to right shunt has been created by the operation

Finally, it is hoped that all this work and controversy will prove of historical interest only for the time is already ripe for repairing the ventricular septal defect, as well as relieving the stricture under direct vision with the aid of hypothermia or some kind of artificial circulation

## PULMONARY ATRESIA

Complete obliteration of the pulmonary valve and root of the main pulmonary artery accounted for 15 of the 900 cases in this series (1 7 per cent) It was always associated with a ventricular septal defect marked over riding of the aortic root and a well developed broncho pulmonary anastomosis

### *HÆMODYNAMICS*

Life depends on the efficiency of the broncho pulmonary anastomosis rarely on the presence of a large patent ductus In those that survive infancy large bronchial arteries join one or more primary or secondary division branches of the pulmonary artery on one or both sides (Allanby *et al* 1950) Mixed venous and arterial blood from the aorta is thus carried to the lungs through the normal pulmonary arterial tree by passing only the main pulmonary trunk A less important peripheral anastomosis between the two circulations also develops The output of both ventricles is expelled entirely through the ascending aorta which is enlarged accordingly The low pulmonary vascular resistance and high feeding pressure ensures a good pulmonary blood flow if the total cross section of the communicating bronchial arteries is around 0 25 sq cm

### *AGE AND SEX*

The average age of the patients in this small series was 11 and the range 3 to 35 years There were two males to one female

### *CLINICAL FEATURES*

Pulmonary atresia resembles Fallot s tetralogy in many ways but it has several distinguishing features which enable it to be recognised at the bed side with ease

Cyanosis clubbing and polycythæmia are usually considerable or gross but not necessarily clinically acyanotic cases are never seen Breathlessness is considerable in two thirds and mild to moderate in one third Squatting occurred in only one quarter of the present series

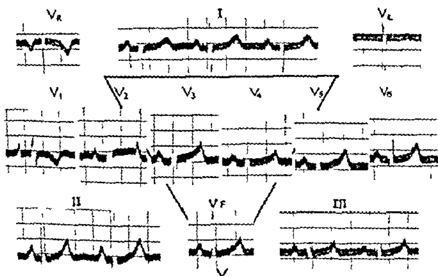



Fig 8 9 —Electrocardiogram in a case of pulmonary atresia showing relatively slight right ventricular preponderance there is a 3 mm P pulmonale in standard lead 2

One quarter also had syncopal attacks sometimes with convulsions in pulmonary atresia such attacks obviously cannot be due to transient functional occlusion of the infundibulum during systole and suggest therefore that pulmonary vasoconstriction or a fall in systemic peripheral resistance is responsible No opportunity to study an attack presented itself

The *physical signs* were like those of Fallot s tetralogy except that instead of a pulmonary ejection murmur which of course was absent there was a continuous murmur in all 15 cases It was best heard just below the clavicle and was bilateral in two thirds of the cases when it was unilateral it was as often on the right side as on the left There is good reason to believe therefore that this murmur is nearly always caused by a proximal broncho pulmonary anastomosis and not by a patent ductus

The electrocardiogram does not differ from that in Fallot s tetralogy (fig 8 9) but the skiagram usually shows a more prominent ascending aorta (fig 8 93) or knuckle Angiocardiography may reveal the broncho pulmonary anastomosis and shows no main pulmonary artery (fig 8 94)

The pulmonary blood flow may be measured very easily for it is only necessary to obtain a sample of blood from the brachial or femoral artery and to measure the oxygen consumption the mixed blood in the arterial sample is the same as that in the pulmonary arteries and pulmonary venous blood may be assumed to be 95 per cent saturated In the few that have been measured the pulmonary blood flow has ranged between [illegible] and 4 litres per minute

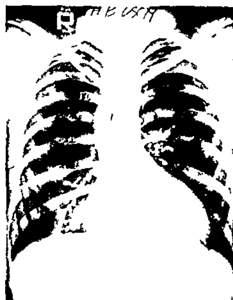


Fig 8 93—Skiagram from a case of pulmonary atresia showing a prominent ascending aorta conspicuous pulmonary bay and pulmonary ischæmia Angiocardiography proved that the aortic arch and dorsal aorta were left sided



Fig 8 94—Angiocardiogram from a case of pulmonary atresia showing dense opacification of the right ventricle and aorta and a large broncho pulmonary anastomotic vessel on the left side

The *prognosis* in those who survive infancy seems much the same as in Fallot s tetralogy

*Surgical treatment* is not nearly so satisfactory as in Fallot s tetralogy, and the mortality is higher Blalock s operation is usually advised if the pulmonary blood flow is below 4 litres per minute Considerable care must be taken not to interfere with the broncho pulmonary shunt particularly if unilateral while constructing the artificial anastomosis

## ABSENT LEFT OR RIGHT BRANCH OF THE PULMONARY ARTERY

From time to time cases are seen in which the pulmonary vascular markings are very light on one side and unduly heavy on the other When there is no kyphoscoliosis and no evidence of unilateral emphysema this usually means congenital absence of the left or right pulmonary artery The whole of the right ventricular output passes down the normal branch as it does following pneumonectomy There is no rise in resting pulmonary artery pressure because the flow is only twice normal but there is less reserve and the pressure may well rise on exercise The ischæmic lung handles about one third of the inspired air but takes up only 6 per cent of the total oxygen uptake (McKim and Wiglesworth 1954)

As a rule the aortic arch is on the side opposite that of the absent pulmonary artery The deficiency may be associated with other congenital anomalies such as Fallot s tetralogy (Nadas *et al* 1953) when it may have an important bearing on the surgical treatment

## TRICUSPID ATRESIA

Tricuspid atresia accounted for 1 5 per cent of the 900 cases analysed here Uncomplicated cases (type I of Edwards and Burchell 1949) have an atrial septal defect or patent foramen ovale through which blood escapes from the otherwise closed right atrium into the left atrium blood reaches the lungs from the left side of the heart through a ventricular septal defect patent ductus or broncho pulmonary anastomosis In addition there may be pulmonary atresia or stenosis valvular or infundibular Complicated cases (type II of Edwards and Burchell 1949) have transposition of the great vessels with or without pulmonary stenosis venous blood entering the left atrium via the foramen ovale mixes with blood from the lungs and passes directly into the pulmonary artery and indirectly into the aorta via a ventricular septal defect In either case the left ventricle does all or most of the work but the lungs are ischæmic in type I plethoric in type II

### *AGE AND SEX*

Of 37 cases mostly collected from the literature 28 died within the first year three within the second year and six between the ages of 2 and 5 (Sommers and Johnston 1951) The average age of the 13 cases described here however was 9 4 years and the range 3 to 17

The sexes are fairly equally represented perhaps with a slight bias in favour of females (M/F=4/5)

### *CLINICAL FEATURES*

Effort intolerance cyanosis clubbing and polycythæmia are invariably considerable or gross squatting is the rule angina occasional and syncope rare

The physical signs include a giant *a* wave when there is a foramen ovale rather than an atrial septal defect a forceful left ventricular cardiac impulse a systolic murmur usually accompanied by a thrill at the base due to ventricular septal defect in over half the cases and a single second heart sound owing to absence of the pulmonary element in the majority Sometimes there is only a trivial aortic flow murmur at the base and a continuous murmur under the left clavicle which in tricuspid atresia is more likely to be caused by a patent ductus than by a broncho pulmonary anastomosis Occasionally the second heart sound is split especially when there is a good sized ventricular septal defect the pulmonary element can be very late when there is associated pulmonary stenosis

Fig 8 95—Electrocardiogram in a case of tricuspid atresia showing considerable left ventricular preponderance

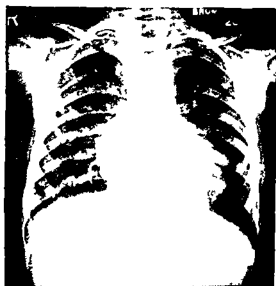


Fig 8 96—Tricuspid atresia showing pulmonary ischæmia with enlargement of the right atrium and left ventricle

The *electrocardiogram* is characterised by a conspicuous P pulmonale averaging 3.5 to 4 mm in amplitude and grade 2 to 3 left ventricular preponderance (fig 8 95)

X *rays* show a combination of pulmonary ischæmia hypoplastic pulmonary artery left ventricular enlargement and dilatation of the right atrium (fig 8 96)

*Angiocardiography* shows diagnostic filling the two atria in high concentration almost simultaneously followed by opacification of the left ventricle and aorta the pulmonary artery remaining invisible or but faintly delineated (fig 8 97)

Cardiac catheterisation is not advised because it can only reveal a giant *a* wave in the right atrium and reversed interatrial shunt findings which do not exclude pulmonary hypertension or stenosis with reversed interatrial shunt Failure to pass the catheter through the tricuspid orifice is no evidence of atresia

The *prognosis* is poor most patients dying in infancy Blalock s or Pott s operation may greatly improve the pulmonary blood flow and so relieve cyanosis and dyspnœa but the shunt adds to the burden of the left ventricle and may lead to heart failure Nevertheless surgical treatment is well worth while despite a fairly high mortality

## TRANSPOSITION OF THE GREAT VESSELS

Transposition the aorta rising anteriorly from the right ventricle and the pulmonary artery posteriorly from the left ventricle occurred in 1 per cent of these 900 congenital cases and in 6 9 per cent of Abbott s series It is a relatively common form of cyanotic congenital heart disease in infancy (Astley and Parsons 1952) but few patients survive Obviously if the two circuits are closed and independent life cannot be sustained Clinical cases therefore must have some means whereby blood is transferred from the systemic to the pulmonary circuit and vice versa ventricular and atrial septal defects usually provide these means blood entering the pulmonary circulation through a ventricular septal defect and leaving it via an atrial septal defect Cases may be further complicated by a high pulmonary vascular resistance pulmonary stenosis tricuspid atresia or other anomalies

### *HÆMODYNAMICS*

If the pulmonary vascular resistance is more or less normal a ventricular septal defect allows venous blood from the right ventricle to enter the left ventricle and pulmonary artery where it mixes with oxygenated blood from the left atrium If these is no atrial septal defect the pulmonary circulation is flooded the only escape being through bronchial anastomotic veins With an atrial septal defect the pulmonary circulation is still plethoric but less so oxygenated blood escaping into the right atrium an



(a)



(b)



( )



(d)

Fig 8 97—Angiocardiogram in a case of tricuspid atresia showing (a) diodone passing directly into th left atrium (1 second) (b) early filling of the left ventricle and aorta (2 seconds) (c) in the second oblique position the left side of the heart and aorta are filled in 2 second (d) at 3 seconds a small left pulmonary artery is becoming visible Note bronchial collaterals in right upper zone in (b)

so to the right ventricle and aorta In otherwise uncomplicated cases there may be hyperkinetic pulmonary hypertension and samples from the pulmonary artery are always more saturated with oxygen than samples from the aorta

If the pulmonary vascular resistance is raised or if there is associated pulmonary stenosis the right to left interventricular shunt is limited or reversed according to the degree of obstruction to pulmonary flow the interatrial shunt is adjusted accordingly being proportionately limited or reversed respectively When the shunts are reversed venous blood from the right atrium enters the left atrium through the atrial septal defect and after mixing with oxygenated blood from the lungs passes on to the left ventricle part of this mixed blood then enters the pulmonary artery and part is shunted into the right ventricle and aorta through the V S D Under these circumstances the pulmonary blood flow is diminished although samples from the pulmonary artery are still more oxygenated than samples from the aorta Tricuspid atresia complicating transposition causes similar reversed shunting through both septal defects

Finally when the defects are large bidirectional shunts may occur at atrial or ventricular level

## *AGE AND SEX*

The average age of the eight patients in this small series was 13 years and the range 3 to 33 years The sexes were equally represented

## *CLINICAL FEATURES*

Effort intolerance, cyanosis, clubbing and polycythæmia were moderate to gross squatting was noticed in only one instance and in only four of 25 cases reported by Campbell and Suzman (1951) Neither angina pectoris nor syncope occurred

The *physical signs* vary according to the chief complication The pulse and venous pressure are usually normal but the jugular pulse may show a small dominant *a* wave The cardiac impulse is usually right ventricular in type a moderate systolic thrust extending from the left sternal edge towards the mid clavicular line In about a quarter of the cases there is no murmur at all in some there is a Roger murmur and thrill and in others a pulmonary ejection murmur and thrill particularly in those with pulmonary stenosis Continuous murmurs are very rare if they occur at all even in those with patent ductus A pulmonary diastolic murmur may be heard when the pulmonary vascular resistance is high and a functional mitral diastolic murmur when there is marked pulmonary plethora The second heart sound also varies according to the nature of the chief complication As a rule it is loud because the root of the aorta is anterior and uncovered by the pulmonary artery In about a third of the cases it is cognisably split and when the pulmo[illegible] ular resistance is ra[illegible]



(a)



(b)



(c)



(d)

Fig 8 97— Angiocardiogram in a case of tricuspid atresia showing (a) diodone passing directly into the left atrium (1 second) (b) early filling of the left ventricle and aorta (2 seconds) (c) in the second oblique position the left side of the heart and aorta are filled in 2 seconds (d) at 3 seconds a small left pulmonary artery is becoming visible Note bronchial collaterals in right upper zone in (b)

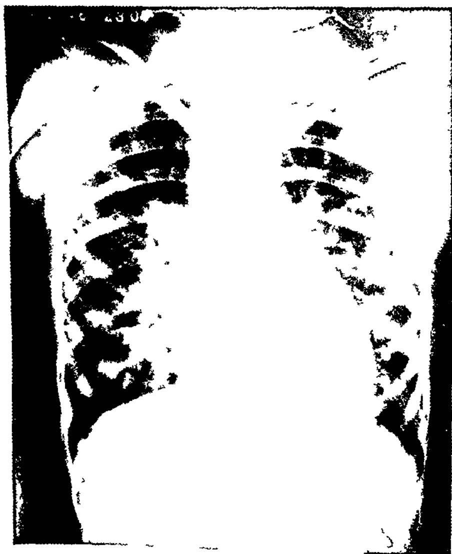


Fig. 8.70—Skiagram of a case of transposition of the great vessels associated with atrial and ventricular septal defects



Fig 8 100—Angiocardiogram in a case of transposition showing a convex arc high up on the left border of the heart this is the ascending aorta and not the pulmonary artery

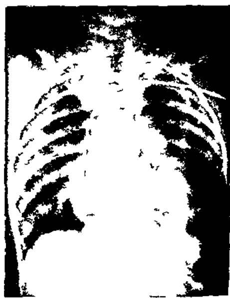


Fig 8 101—Case of transposition of the great vessels showing the typical position of a catheter which has been passed up the ascending aorta and round the aortic arch

to the nature of the associated anomalies As a rule there is a left to right shunt at atrial level if there is an atrial septal defect and a right to left shunt at ventricular level with ventricular septal defect but either shunt may be bidirectional or reversed particularly if there is a raised pulmonary vascular resistance or pulmonary stenosis with tricuspid atresia both shunts are entirely reversed Pressures in the right ventricle and pulmonary artery depend on the pulmonary blood flow the pulmonary vascular resistance and the degree of pulmonary stenosis if present The pulmonary blood flow is high in relatively uncomplicated cases, even when the shunts are small for there is a large volume of oxygenated blood permanently trapped in the pulmonary circulation it may be only slightly in excess of normal however when the pulmonary vascular resistance is high or when there is severe pulmonary stenosis

## *DIFFERENTIAL DIAGNOSIS*

The triad comprising central cyanosis unquestionable pulmonary plethora and right ventricular dominance usually means transposition of the great vessels or *total anomalous pulmonary venous drainage* into the right side of the heart and these two can usually be distinguished radiologically *Persistent truncus* with cyanosis and pulmonary plethora is at once recognised by the large left ventricle

When pulmonary plethora is unconvincing because of associated pul

monary stenosis there may be great clinical difficulty in distinguishing transposition from *Fallot's tetralogy* with a relatively good pulmonary blood flow in fact the only real differences between them are the degree of cyanosis which in transposition is considerable and in Fallot's tetralogy of this kind slight and the size of the heart which is usually larger in transposition If angiocardiography shows no filling of the pulmonary artery *pulmonary atresia* may be diagnosed in error but this mistake should not be made at the bedside

When pulmonary plethora is doubtful because the pulmonary vascular resistance is raised transposition is commonly confused with *Eisenmenger's complex* Genuine dilatation of the pulmonary artery favours Eisenmenger's complex but angiocardiography or cardiac catheterisation may be necessary to establish the diagnosis with certainty

## *PROGNOSIS*

The average duration of life in 123 cases with associated anomalies of the kind described above was 19 months (Hanlon and Blalock 1948) without such associated anomalies life is impossible The patients in the present series however had already survived infancy and their ages show that with good communications between the two circulations the immediate outlook is far from hopeless 9 out of 25 cases of probable transposition reported by Campbell and Suzman (1951) were between 6 and 18 years of age the rest being under 5

## *TREATMENT*

So far attempts to improve the efficiency of communications between the two circulations such as the creation of an artificial atrial septal defect (Blalock and Hanlon 1950) have proved disappointing Surgical correction of the transposition itself with the aid of some form of artificial circulation to the brain is still in the experimental stage

# PERSISTENT TRUNCUS ARTERIOSUS

Persistent truncus results from failure of development of the aorto pulmonary septum so that a single large vessel arises from both ventricles The solitary valve usually has four cusps and a ventricular septal defect is inevitable The pulmonary arteries should arise from the common trunk and if they fail to do so the probable diagnosis is pulmonary atresia

Persistent truncus is a very rare anomaly and there was but one proved example amongst the 900 congenital cases reported here

## *HAEMODYNAMICS*

If the pulmonary vascular resistance is normal the pulmonary circulation is flooded to its maximum capacity because the pulmonary arteries are filled at systemic pressure The left ventricle enlarges greatly to

the torrential flow that is received from the lungs and the right ventricle hypertrophies to adapt itself to systemic conditions The truncus itself may be very large not simply because it represents two great vessels but because it may have to carry an enormous flow Cyanosis may be minimal because mixed venous blood from the systemic and pulmonary circulations is about five sixths pulmonary and therefore likely to be well over 80 per cent saturated

A normal pulmonary vascular resistance however may be unusual in cases that survive infancy and physiological studies may well reveal a resistance in the Eisenmenger range (around 17 units) in the majority Pulmonary and systemic blood flows would then be balanced and the two ventricles would perform identical work Cyanosis should be considerable in this group

If the pulmonary resistance rose much above systemic level the pulmonary blood flow would be diminished and the left ventricle would perform less work than the right Such cases would be intensely cyanosed and similar physiologically to pulmonary atresia

## *CLINICAL FEATURES*



Fig 8 102—Case of persistent truncus arteriosus showing marked pulmonary plethora a conspicuous bay in the region of the pulmonary artery and considerable enlargement of the heart shadow due chiefly to dilatation of the left ventricle

Persistent truncus with a relatively normal pulmonary vascular resistance is characterised by slight central cyanosis clubbing and polycythæmia and relatively slight effort intolerance until there is left ventricular failure the pulse may be water hammer in quality and there may be a small dominant *a* wave in the jugular venous pulse but the venous pressure is usually normal until heart failure develops the left ventricle is thoroughly enlarged and hyperdynamic the right less so there is usually a systolic ejection murmur with or without thrill at the base a loud single second sound and sometimes a basal diastolic murmur due to a leaking quadricuspid valve the incompetence affecting both ventricles A functional mitral diastolic murmur would be expected A continuous broncho-pulmonary anastomotic murmur means pulmonary atresia, not persistent truncus

The electrocardiogram shows conspicuous Q waves and tall R waves in leads $V_5$ and $V_6$ and perhaps a secondary R wave in leads $V_1$ and V from right ventricular hypertrophy as well The P wave may be normal bifid and widened from left atrial enlargement or a little tall and sharp from right atrial hypertrophy

The skiagram shows gross pulmonary plethora absence of the pulmonary arc a conspicuous ascending aorta and considerable enlargement of the heart shadow particularly the left ventricle (fig 8 102)

When the pulmonary vascular resistance is high the clinical features are more like Eisenmenger s complex Cyanosis and clubbing are much more conspicuous and dyspnœa more severe The pulse loses its water hammer quality The ventricles are about equal in size and clinically the right may be dominant Auscultatory signs are unchanged except that a mitral diastolic murmur would not be expected The electrocardiogram shows a P pulmonale and considerable right ventricular preponderance Radiologically there is less pulmonary plethora (if any) and less cardiac enlargement whilst the left ventricle is no longer hyperdynamic

## *DIFFERENTIAL DIAGNOSIS*

Many cases of persistent truncus present clinical electrocardiographic and radiological features that lie somewhere between the two prototypes described above Essentially the pattern is one of central cyanosis enlargement of both ventricles particularly the left a single second heart sound absence of the pulmonary arc and pulmonary plethora This combination admits of no other diagnosis

*Pulmonary atresia* with its continuous broncho pulmonary anastomotic murmur small quiet left ventricle and obvious pulmonary ischæmia presents an entirely different picture and should not enter into the differential diagnosis at all

*Eisenmenger s complex* can nearly always be distinguished by the dilated pulmonary artery *Transposition* alone presents any real difficulty Both it and persistent truncus have central cyanosis pulmonary plethora and a hyperdynamic left heart but in transposition the second heart sound may be split the ascending aorta is inconspicuous or in its wrong position and the right ventricle is nearly always dominant

*Angiocardiography* should reveal the essential anatomical arrangement in persistent truncus On *cardiac catheterisation* the pathognomic finding is to enter either pulmonary artery from the ascending aorta In the case studied in this series there was no difficulty in accomplishing this pulmonary artery aortic and right ventricular systolic pressures were identical the oxygen saturation of samples was 48 per cent in the right atrium 58 per cent in the right ventricle and 72 per cent in the truncus proving the presence of a left to right shunt at ventriculo aortic level

## *PROGNOSIS AND TREATMENT*

Cases with a low pulmonary vascular resistance probably die from cardiac failure in infancy When the pulmonary resistance is raised sufficiently to protect the lungs from over flooding and the left ventricle from overwork but not so much as to diminish the pulmonary blood flow the outlook is not so bad and may be more like that in Eisenmenger s complex As a general rule however patients who survive infancy die from congestive heart failure in childhood or adolescence No surgical treatment is possible

## TOTAL ANOMALOUS PULMONARY VENOUS DRAINAGE

Embryologically a single pulmonary vein originally joins the sinus venosus The superior horns of the sinus ducts of Cuvier and lower part of the anterior cardinal veins become the superior vena cava on the right side and the oblique vein of the left atrium (vein of Marshall) and coronary sinus on the left A persistent left superior vena cava therefore joins the oblique vein of the left atrium and enters the right atrium via the coronary sinus

The formation of the interatrial septum separates that part of the sinus venosus that the pulmonary vein joins from the rest of the right atrium Since there are normally four pulmonary veins joining the left atrium it is clear that the original single pulmonary venous trunk becomes absorbed into the sinus venosus It is not at all difficult for one or other of the right pulmonary veins to find itself entering the primitive atria on the wrong side of the growing septum *Partial anomalous pulmonary venous drainage* arising in this way has already been described and is not infrequently associated with atrial septal defect

In total anomalous pulmonary venous drainage the original single pulmonary vein may join up with almost any other part of the sinus venosus system thus it is found entering the coronary sinus in 19 per cent left superior vena cava in 43 per cent, right superior vena cava in 12 per cent right atrium in 14 per cent and even the inferior vena cava sometimes (Keith *et al* 1954) When it enters the coronary sinus there is usually a left superior vena cava as well and this invariably communicates with the left innominate vein and so with the right superior vena cava through which the pulmonary venous blood eventually drains into the right atrium

## *HÆMODYNAMICS*

All the blood from the lungs enters the right atrium by one route or another, and after mixing with blood from the systemic veins passes to the left ventricle via an atrial septal defect or foramen ovale, and to the right ventricle through the tricuspid valve Samples from all cardiac chambers are therefore identical

Since the right ventricle offers less resistance to filling than the left and since the tricuspid valve opening is usually wider than that in the atrial septum more blood enters the right ventricle than the left The pulmonary blood flow is therefore increased, and the systemic output tends to be low This also means that the majority of blood entering the right atrium is already 95 per cent saturated so that the mixed venous sample arriving in the left ventricle is likely to be around 85 per cent saturated Central cyanosis is therefore slight or even absent at rest If the pulmonary vascular resistance is raised the right ventricular diastolic pressure tends to rise the right to left interatrial shunt increases the pulmonary blood flow is reduced and cyanosis may then be intense but this is unusual

There were only two proved examples of this rare anomaly in the present series But five typical cases were described by Snellen and Albers (1952) four by Gardner and Oram (1953) six by Whitaker (1954) and fourteen by Keith *et al* (1954) who also reviewed 45 other cases culled from the literature A good earlier review is that by Brody (1942)

The majority of cases in the literature occurred in infancy 80 per cent proving fatal within the first year of life

The sex ratio is three males to two females

## *CLINICAL FEATURES*

There is a very great discrepancy between the high infant mortality in this condition and the relatively good health of many classical cases described in adolescents and young adults The explanation of course lies with the behaviour of the foramen ovale or with the size of the inter atrial communication Many infants die because the foramen ovale becomes sealed off despite the higher pressure on the right side of the atrial septum (Taussig 1947) Others in whom the foramen ovale remains patent have to depend on this small opening for the whole of their systemic blood flow On the other hand patients with a good sized atrial septal defect are likely to have an adequate right to left interatrial shunt and fare relatively well (Snellen and Albers 1952) The syndrome to be described is that seen in children and young adults with good interatrial shunts

Effort intolerance is not severe and cyanosis is minimal unless the pulmonary vascular resistance is high. Recurrent bronchitis may occur as in other cases with plethoric lungs Physical development is poor

The peripheral pulse is small and the jugular venous pressure and pulse normal unless the pulmonary vascular resistance is raised (Eisenmenger reaction) or the right heart fails

The central cardiac signs are very similar to those of atrial septal defect the left ventricle is impalpable, the right thrusting and hyperdynamic and an impulse may be felt over the pulmonary artery there is nearly always a pulmonary ejection murmur in the third left space often accompanied by a faint or moderate thrill and the second heart sound is widely split and presumably unaltered by respiration the intensity of $P_2$ no doubt

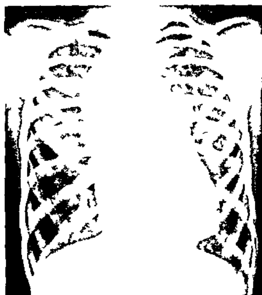


Fig 8 103—Typical figure of eight appearance in a case of total anomalous pulmonary venous drainage into the left superior vena cava

varies with the pulmonary artery pressure pulmonary incompetence occurs in a minority A superior vena caval hum uninfluenced by posture or compressing the root of either jugular vein may be heard in the aortic area in about a quarter of the cases (Snellen and Albers 1952) A functional mid diastolic murmur caused by interatrial or tricuspid turbulence was heard in three out of four cases reported by Gardner and Oram (1953) and in two out of six cases described by Whitaker (1954)

The *electrocardiogram* shows a partial right bundle branch block pattern as in atrial septal defect

The *skiagram* reveals a figure of eight appearance (fig 8 103) the upper half of which represents the dilated left superior vena cava left innominate vein and right superior vena cava as first clearly illustrated by Taussig (1947) and emphasised by Snellen and Albers (1952) Other features include a small aorta, pulmonary plethora and dilatation of the pulmonary artery right ventricle and right atrium as in atrial septal defect

Routine *angiocardiography* shows more or less simultaneous filling of both sides of the heart the reversed shunt being at atrial level after passing through the lungs contrast medium enters the left superior vena cava A clearer picture of the anomalous pulmonary venous drainage is obtained if diaginol is injected directly into the pulmonary artery

The *physiological findings* are also pathognomonic for samples from all intracardiac chambers and from both the aorta and pulmonary artery are identical or if the interatrial communication cannot be penetrated then at

least the arterial sample is the same as those from the right side of the heart S V C samples are more saturated than those from the right atrium and much more so than those from the I V C If the catheter is passed up the left subclavian vein it may enter the left superior vena cava and then fully saturated pulmonary venous blood may be obtained The pulmonary blood flow is usually over 15 litres per minute unless the pulmonary vascular resistance is raised the systemic flow averaging around 4 litres per minute The pulmonary artery pressure is usually raised moderately owing to the very great flow

## *DIFFERENTIAL DIAGNOSIS*

The combination of slight central cyanosis otherwise typical clinical features of a large atrial septal defect with direct shunt the addition sometimes of a basal venous hum and the pathognomonic figure of eight skiagram, can hardly be mistaken for any other condition At the bedside however, atrial septal defect with bidirectional shunt despite the absence of a high pulmonary vascular resistance and cases of single atrium present very similar features Selective angiocardiography and cardiac catheterisation should establish the diagnosis with certainty

## *PROGNOSIS AND TREATMENT*

As already stated if the foramen ovale closes or tends to close infants necessarily die but if there is a good sized atrial septal defect the outlook is fair most such cases reaching adult life although very few have been reported over 30 years old

Surgical transplantation of the misplaced pulmonary vein has yet to be accomplished

## ANOMALOUS DRAINAGE OF THE S V C OR I V C INTO THE LEFT ATRIUM

A rare but interesting anomaly seen only once in this series is anomalous drainage of the superior vena cava into the left atrium The patient was a girl aged 10 with life long slight central cyanosis and grade I effort intolerance There were no obviously abnormal physical signs but the left ventricle was a little thrusting for it was working harder than the right and the second heart sound was single A being slightly later and P earlier than normal The electrocardiogram showed an S wave in lead V measuring 28 mm but was otherwise normal The skiagram looked normal Angiocardiography however revealed anomalous superior vena cava drainage into the left atrium diaginol passing directly into the left side of the heart without entering the right atrium at all (fig 8 104a) When diaginol was injected into the saphenous vein the inferior vena cava was seen to join the right atrium normally (fig 8 104b) On cardiac





(a) (b)

Fig 8 104—Angiocardiogram from a case of anomalous drainage of the superior vena cava into the left atrium (a) showing diaginol in the superior vena cava left atrium left atrial appendage left ventricle and aorta (b) showing diaginol in the right atrium right ventricle and pulmonary arteries after being injected into the saphenous vein the top of the right atrium ends blindly

catheterisation it was not at first realised that the catheter had entered the left atrium directly its immediate passage into a pulmonary vein being attributed to the presence of an atrial septal defect when a ventricle was entered the bluish sample obtained (70 per cent saturated) suggested that it was the right ventricle although its systolic pressure was at systemic level and it was of course the left

Surgical correction should be possible but the disability was too slight in this case to warrant interference

A good example of a case in which the *inferior vena cava drained directly into the left atrium* was reported by Gardner and Cole (1955) This patient died suddenly at the age of 32 and necropsy showed an old posterior cardiac infarct in addition to the anomaly under consideration The clinical features of the congenital anomaly were essentially the same as in the case of anomalous superior vena cava drainage described above there being central cyanosis without other abnormal physical signs and the skiagram also looked normal The electrocardiogram was influenced by the old infarct

## COR TRILOCULARE BIATRIATUM

Hearts with two normal atria and a single ventricle are rare (1 3 per cent of Abbott s 1,000 cases) but not so rare as two chambered hearts Trans

position of the great vessels the aorta lying anteriorly and a little to the right the pulmonary artery posteriorly and a little to the left without any spiral arrangement is usually associated A rudimentary outflow chamber from which either the aorta or pulmonary artery (or both) may arise is sometimes found (Taussig 1947) and pulmonary valve stenosis is not uncommon The famous Holmes heart was from a moderately cyanosed man of 23 who died after a bout of dissipation for which he had a turn The pulmonary artery arose anteriorly from a small rudimentary outflow chamber protected proximally by an infundibular stenosis which clearly limited the blood flow to the lungs the aorta arose posteriorly from the body of the common ventricle there being no transposition in this case (Abbott 1901)

Complete mixing of systemic and pulmonary venous blood takes place in the common ventricle from which it is ejected at systemic pressure If the pulmonary vascular resistance were normal the lungs would be flooded and survival unlikely as in persistent truncus arteriosus therefore fœtal pulmonary vasoconstriction is usually maintained and this regulates the amount of blood sent to the lungs (Rogers and Edwards 1951) Pulmonary stenosis usually valvular occurs in about a quarter of all cases (Campbell Reynolds and Trounce 1953) and performs a similar service When the lungs are flooded cyanosis is minimal or absent but the single ventricle which has to perform double work under the best conditions becomes grossly overloaded When the aorta arises from a rudimentary outflow chamber with proximal stenosis extreme pulmonary vasoconstriction would be necessary to provide an adequate systemic blood flow and prevent gross flooding of the lungs

## *AGE AND SEX*

Although the majority die in infancy probably as a result of other anomalies or because the pulmonary arterioles fail to regulate the pulmonary flow satisfactorily about 20 per cent reach adult age the oldest recorded being 56 (Mehta and Hewlett, 1945)

The sex ratio is 3 : 1 in favour of males (Campbell Reynolds and Trounce 1953)

## *CLINICAL FEATURES*

The degree of dyspnœa and cyanosis is probably proportional to the pulmonary vascular resistance or to the degree of pulmonary stenosis when that is present Nevertheless slight to moderate cyanosis is physiologically desirable for acyanotic cases are far more likely to die in infancy from heart failure due to overloading of the single ventricle secondary to a flooded pulmonary circulation

No good descriptions of the physical signs of patients with single ventricle are available in the medical literature but most have a basal

systolic murmur with or without thrill and this is probably a pulmonary ejection murmur as in Eisenmenger's complex which these cases imitate closely When there is associated pulmonary stenosis the physical signs are presumably more like those of Fallot's tetralogy

The electrocardiogram is variable normal Q waves are usually seen in antero lateral chest leads or in one of the left sided unipolar limb leads despite the absence of the interventricular septum as in the univentricular heart of fishes and frogs (Kisch 1949) otherwise the graph is apt to show changes which might ordinarily be more easily attributed to clockwise or anticlockwise rotation In cases with pulmonary stenosis Campbell Reynolds and Trounce (1953) could not distinguish the graph from that seen in Fallot's tetralogy

The skiagram resembles that in Eisenmenger's complex when there is pulmonary hypertension and Fallot's tetralogy when there is pulmonary stenosis but in both types the heart is apt to be larger

Few physiological studies have yet been reported In uncomplicated cases the findings are similar to those of Eisenmenger's complex with bidirectional shunt but there is no difference between samples from the aorta and from the pulmonary artery When there is pulmonary stenosis the findings are like those in Fallot's tetralogy in respect of the pressures recorded and like uncomplicated single ventricle in respect of the samples

Angiocardiography shows simultaneous filling of the aorta and pulmonary artery as in Eisenmenger's complex and Fallot's tetralogy but with good technique it should be possible to demonstrate complete opacification of the whole ventricular shadow from the right atrium the left atrium remaining translucent

## PROGNOSIS AND TREATMENT

The outlook is fair in those who survive infancy and depends on how satisfactorily the pulmonary circulation can be regulated by the pulmonary vascular resistance or the pulmonary stenosis

Surgical treatment is impossible in those with pulmonary hypertension and usually inadvisable in those with pulmonary stenosis unless the pulmonary blood flow is obviously inadequate

## COR BIVENTRICULARE TRILOCULARE

Hearts with a single atrium and two ventricles are exceptionally rare They cannot be distinguished clinically from those rare cases of atrial septal defect with bidirectional but predominantly left to right interatrial shunt and a normal pulmonary vascular resistance Cardiac catheterisation however, should show identical samples from all cardiac chambers beyond the superior vena cava and inferior vena cava as if all the pulmonary veins drained directly into the right atrium The pulmonary blood flow is greatly increased because the right ventricle offers less resistance to filling than the left

The prognosis is similar to that in cases of gross atrial septal defect the few examples reported usually dying from heart failure in childhood or adolescence (Brown 1950)

No surgical treatment is possible unless an artificial septum could be created

## COR BILOCULARE

A two chambered heart is probably the rarest of all congenital cardiopathies and practically never occurs without other anomalies (Brown 1950) Physiologically the situation should be precisely the same as that in a heart with two atria and a single ventricle except that mixing of pulmonary and systemic venous blood takes place in the atrium instead of the ventricle

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CHAPTER IX

# RHEUMATIC FEVER AND ACTIVE RHEUMATIC CARDITIS

RHEUMATIC fever is a particular form of polyarthritis following streptococcal infection its hall marks are pancarditis chorea, sub cutaneous nodules and erythema marginatum. It may be acute sub acute or chronic

## INCIDENCE

According to the 1927 report of the Child Life Committee of the Medical Research Council Social Conditions and Acute Rheumatism 10 to 15 per cent of all children at 12 years of age in England are affected by rheumatism Of 22 800 children under 15 years of age card indexed by the London County Council 2 6 per cent had had rheumatic fever (Bach *et al* 1939) The crude annual death rate from rheumatic fever declined from 67 per million persons in 1901 to 22 per million in 1937 (Glover 1939) During 1937 according to Glover rheumatic fever accounted for 2 3 per cent of all deaths in children between the ages of 5 and 9 years

The disease is rare in infancy and in old age and is most common in childhood and adolescence attacking the poor rather than the rich and having an incidence climatically and geographically parallel to streptococcal tonsillitis (Coburn 1931) The peak incidence is in children between the ages of 6 and 12 particularly during the months of October November and of January February Apart from arachnodactyly there is no evidence that a particular physical type is predisposed to rheumatic fever (Hill and Allan 1929) *but hereditary predisposition is now accepted* (Wilson 1940 Wilson and Schweitzer 1954)

## THE NATURE OF THE RHEUMATIC STATE

There is no evidence as yet that rheumatic fever is caused directly by any infective agent Cultures from blood joint fluid pericardial or pleural effusions and from affected tissues are bacteriologically sterile and filtrates from similar samples are incapable of transmitting the disease when inoculated into animal or man There is still perhaps a remote possibility that a virus is responsible but the known facts are against it

On the other hand the evidence that rheumatic fever is intimately related to streptococcal infection is beyond dispute The relationship was first propounded by Poynton and Payne in 1900 They isolated a diplococcus from blood and other cultures and produced polyarthritis and carditis injecting it into animals but the lesions were shown later to be infe

not rheumatic However they confirmed the observation of Haig Brown (1886) that rheumatic fever was nearly always preceded by streptococcal sore throat the latent interval being 10 to 20 days (Poynton and Payne 1913) The most convincing proof of this was later given by Schlesinger (1930) The responsible organism is always a hæmolytic streptococcus (Collis 1931) As previously stated the incidence of rheumatic fever follows closely the geographic social and seasonal incidence of streptococcal tonsillitis (Coburn 1931) and small epidemics of rheumatic fever in closed communities always follow epidemics of streptococcal sore throat (Glover 1930) Culpable streptococci belong serologically to group A, and may liberate powerful erythrogenic toxins and hæmolysins—in fact they are often scarlatinal strains (Coburn and Pauli 1935) Serum from the subjects of rheumatic fever agglutinate these strains in high titre and anti strepto coccal hæmolysins (antibodies excited by the antigenic properties of strepto coccal hæmolysins) have been found in high titre in the early stages of practically all cases of active rheumatic fever, whether or not a history of streptococcal infection is obtained (Todd 1932) Most of these observa tions have been confirmed independently by other workers notably Griffith (1935) Sheldon (1931) and Bradley (1932)

It is now generally believed that rheumatic fever is an abnormal tissue reaction to the products of hæmolytic streptococcal infection in a sensitised individual A number of other observations supports this hypothesis Thus allergic polyarthritis with a latent interval of 8 to 9 days, may follow the injection of foreign serum polyarthritis may similarly follow gonococcal dysenteric and other bacterial infections in individuals sensitised by pre vious attacks associated skin lesions in rheumatic fever, such as erythema multiforme strongly suggest allergy The experimental work of Rich and Gregory (1943 1944) who succeeded in producing carditis of the rheu matic type in rabbits by injecting horse serum and of Cavelti (1947) who was equally successful in rats which were injected with an antigen con sisting of killed streptococci and heart or connective tissue emulsion provides convincing evidence of the existence of an allergic form of carditis which may be related to the streptococcus and which at least resembles that seen in rheumatic fever Finally, Murphy and Swift (1949) produced microscopic lesions in the hearts of rabbits closely resembling those seen in rheumatic carditis, by repeated intradermal injections of group A beta hæmolytic streptococci

The relationship between rheumatic fever and rheumatoid arthritis is still uncertain Serum from patients with rheumatoid arthritis commonly agglutinates all strains of hæmolytic streptococci in high dilution (Dawson *et al* 1932) but does not, as a rule, contain the high titre anti hæmolysins characteristic of rheumatic fever (Stuart Harris 1935) nevertheless the anti streptolysin titre is much higher than in normal controls (Goldie and Griffiths 1936) Whether there is any essential difference between the pathology of the affected joints and in the structure of subcutaneous nodules

in the two conditions other than those which might be due to the age of the patient or to the chronicity of the lesion, is still a matter of controversy (Goldie 1936) The incidence of a rheumatic type of cardiac lesion in rheumatoid arthritis is difficult to assess from the literature but appears to range between 3 and 30 per cent in clinical studies and between 25 and 66 per cent in post mortem studies (Rogen 1947) These figures are probably too high The subject is well reviewed by Bywaters (1950)

## PATHOLOGY

In a fulminating attack which ends fatally within two or three weeks tissue microscopy reveals only non specific lesions consisting of œdema fragmentation of collagen leucocytic infiltration hyperæmia and capillary hæmorrhage (Coburn 1933) Similar lesions may occur in most acute infections toxæmias and allergic states and represent the Arthus phenomenon (Werner 1938) Many tissues are so affected particularly the synovial membranes of the larger joints the pericardium myocardium, and endocardium the pleura and lung Petechiæ may be seen clinically in the skin (purpura rheumatica) or in the ocular fundi and at autopsy they are often most obvious in the pericardium and pleura Inflammatory œdema of soft tissues may be seen clinically independent of arthritis Effusion into the large joints and sometimes into the pericardial or pleural cavities, is characteristic and is the best example of the exudative type of lesion

The specific rheumatic lesion however is proliferative and occurs rather later it is characterised by the Aschoff node (Aschoff 1904) This is a small collection of large often multinucleated reticulo endothelial cells mixed with lymphocytes and plasma cells surrounding a necrotic collagenous centre there is also fibroblastic proliferation Whilst it is in no sense perivascular it lies in close relationship to a vessel This lesion is particularly well seen in the myocardium Another example of the proliferative lesion is the subcutaneous nodule which may be regarded as an aggregation of Aschoff nodes with fibroblastic tissue predominating (fig 901)

Occasionally vascular lesions are found in the viscera which show all the features of panarteritis Involvement of the cerebral pulmonary coronary and mesenteric arteries has been described (Ritchie 1939) Secondary thrombosis may occur but is uncommon Later the media may become calcified

Rheumatic inflammation of the heart valves is a true valvulitis, the baneful agent entering the valve through the minute vessels which supply it (Shaw 1929) There has been considerable disagreement concerning the vascularity of normal and diseased heart valves Langer (1887) first demonstrated the dependence of valvular blood vessels upon the presence of muscle he showed that vessels and muscle fibres reached the free edge of the valve in the fœtus and new born child but soon regressed also th

diseased valves were frequently vascularised whereas normal adult valves were not Gross and Kugel (1921 1925–26 1927–28 1931) who studied the coronary circulation in detail by means of radiography after injecting a barium sulphate gel confirmed Langer s observations They also found that in the fœtus the pulmonary valve was the one best provided with muscle and blood vessels whereas in children it was the aortic cusp of the mitral valve The belief that endocarditis *in utero* usually affected the pulmonary valve whereas in children it usually affected the mitral valve, thus appeared to have a rational basis The decreasing incidence of valvulitis as age advanced was similarly explained More recent work based on the



Fig 9 01—Rheumatic nodules in the occipital aponeurosis

injection of Indian ink instead of barium gel however has thrown doubt on these conclusions Wearn *et al* (1936) for instance found capillaries in the valves of 84 per cent of seventy four normal hearts and were unable to correlate the relative incidence of endocarditis of a given valve with the frequency with which it contained blood vessels Thus the mitral valve was vascularised in 66 per cent the tricuspid in 64 per cent the pulmonary in 28 per cent and the aortic in 16 per cent It is possible that the factor governing the relative frequency with which each valve is involved is simply the degree of natural trauma to which each is exposed In a child of 10 for example with a systemic blood pressure of 100/60 mm Hg and a pulmonary blood pressure of 15/5 mm Hg the load supported by the mitral, aortic, tricuspid and pulmonary valves is in the proportion of 100

60, 15 and 5 mm Hg respectively. According to Cabot (1926) the mitral valve is involved in 85 per cent of cases, the aortic in 44 per cent, the tricuspid in 10 to 16 per cent, and the pulmonary in 1 to 2 per cent, which is very close to the relative frequencies that would be predicted if the above hypothesis were correct.

In the acute stage of rheumatic inflammation the valve is *œdematous* and soon shows signs of damage just proximal to its free edge where the cusps come into apposition, i.e. at the site of maximum natural trauma. Small thrombi form on the valve at this site giving rise to a ridge or to a row of small pink nodules. As the inflammation subsides, secondary sclerosis follows and results particularly in fusion of the cusps at the critical areas of tendon insertion (Brock, 1952) as described in the next chapter. Sclerosis may affect the cusps themselves, the chordæ tendineæ, the papillary muscles and the mitral ring in varying degree. When the damage is slight, *simple fusion of the cusps (mitral stenosis) is the most likely* consequence; when the damage is considerable all parts of the valve mechanism become thickened and disorganised, and serious mitral incompetence develops. According to Carey Coombs (1924) mitral stenosis usually takes 2 to 8 years to develop, the stricture increasing very slowly over the years. Mitral incompetence usually begins at once during the stage of active inflammation, and may progress rapidly in severe cases, abetted by *dilatation of the mitral ring as the left ventricle dilates* in response to its increasing load or as a result of myocarditis; once heavy scarring of the mitral valve is well established, however, the degree of incompetence is unlikely to increase further, perhaps rather to the contrary.

Fusion of the aortic cusps, leading to aortic stenosis, also results from secondary sclerosis and usually takes several years to develop, the stricture then *increasing gradually over the years.* Aortic *incompetence*, on the other hand, like mitral incompetence, usually begins during the active stage of the disease, and may progress rapidly in severe cases. Slight or moderate leaks may increase gradually over the years as a result of secondary sclerotic changes, or if the latter cause increasing fusion of the cusps early incompetence may be replaced by dominant stenosis.

## CLINICAL FEATURES

In childhood, the heart often bears the brunt of the attack, and indeed the joints may escape entirely. Once the heart has been involved, however, carditis or valvulitis should be assumed in all subsequent attacks; the increased vascularity of a valve which has been subjected to rheumatic inflammation may partly explain this tendency to recurrence. If the first attack occurs over the age of 21, carditis *is unlikely*, and becomes progressively rare with advancing years, although it may still occur even in old age. Polyarthritis, on the other hand, becomes increasingly common

Of 588 rheumatic children studied in detail by Ash (1948), 58 per cent presented first with polyarthritis 8 per cent with subacute rheumatism 19 per cent with chorea, and 15 per cent with isolated rheumatic carditis About one quarter of acute cases have evidence of pre existing rheumatic heart disease when first seen (joint report 1955)

The diagnosis of rheumatic carditis is based on three major issues upon signs of some inflammatory process upon evidence that this process is rheumatic and upon proof of cardiac involvement

## *SIGNS OF SOME INFLAMMATORY PROCESS*

These are fever, leucocytosis and elevation of the erythrocyte sedimentation rate Fever may be of any degree but is *usually moderate or high initially in children* and moderate or low *grade in adults it is irregular in* type and inclined to relapse it may last only a few days or it may continue for months The temperature is normal in subacute rheumatism, and may be normal when polyarthritis is still active in acute attacks Leucocytosis is slight to moderate in the early phase of acute rheumatic fever, figures of 10 000 to 15 000 white cells per c mm being the rule The differential count may show a slight relative increase of polymorphs, but is often normal In subacute rheumatism the total count is commonly between 7 000 and 10 000 per c mm The sedimentation rate is by far the most valuable evidence of some active inflammatory process and is often remarkably high when there are no other signs Weekly readings have proved a *reliable index of the course of the disease and of the degree of activity* In less *than 5 per cent of cases the test is valueless* the E S R remaining *normal* throughout the illness

It will be appreciated that these three features are non specific they point to some inflammatory process but they do not determine its nature Secondary anæmia and loss of weight or failure to gain weight may be regarded in a similar light According to Cochran (1951) the normocytic orthochromic anæmia is often apparent rather than real for it may result from hæmodilution the plasma volume being increased as originally observed by Bradley (1938)

## *EVIDENCE THAT THE INFLAMMATORY PROCESS IS RHEUMATIC*

(i) *Polyarthritis* Non suppurative polyarthritis with sterile effusions into the large joints is characteristic Involved joints may be painful swollen hot, flushed and tender on the other hand slight effusion into a knee joint may be detected when there are no other signs or symptoms or the patient may complain of joint pains when there are no signs as in subacute rheumatism The older the patient the more often are the small joints affected and it becomes increasingly difficult to distinguish rheumatic fever from rheumatoid arthritis *Pains and effusions tend to flit from joint to joint* one recovering as another is *involved but not necessarily* Occasionally one

knee or other large joint alone is inflamed especially if previously injured and may remain so for weeks or even for months but minimal pains elsewhere may suggest its true nature Other forms of what is thought to be allergic polyarthritis such as the dysenteric variety may be indistinguishable except on other grounds For example dysenteric polyarthritis is proclaimed by associated conjunctivitis and urethritis and by its relation to dysentery

In subacute rheumatism recurrent joint pains occur without effusion and usually without fever or leucocytosis but the sedimentation rate is raised Growing pains confined to the hips knees or ankles mean subacute rheumatism growing pains described in the muscles ligaments or tendons probably do not (Hawksley 1939)

(2) *Relationship to streptococcal infection* The diagnosis is favoured if the symptoms follow a streptococcal sore throat or some other streptococcal infection, including scarlet fever There is a latent interval of 1 to 3 weeks, usually 10 to 14 days. The significance of this relationship cannot be overstressed It appears to be fundamentally the same as the relationship between dysenteric polyarthritis and acute bacillary dysentery or between gonococcal polyarthritis and gonorrhœa Opportunity to study the dysenteric form was afforded by its frequency amongst the troops in North Africa and Italy in the second world war It was characterised by acute polyarthritis involving the large joints by resistance to salicylates by prolonged activity averaging about three months and by associated conjunctivitis and urethritis Joint effusions were sterile and cultures from the conjunctiva and urethra yielded no pathogenic organisms The provocative attack of dysentery was often abortive or very mild and the latent period 10 to 14 days A previous attack of dysentery was invariable and was usually untreated The evidence suggested that a fairly high degree of immunity was necessary for the development of the syndrome Gonococcal polyarthritis was equally common and behaved similarly, except that tenosynovitis replaced conjunctivitis and urethritis was primary The facts suggest that rheumatic fever is streptococcal polyarthritis and bears the same relationship to the streptococcus as does *dysenteric polyarthritis to the dysentery* bacilli and gonococcal polyarthritis to the gonococcus but instead of conjunctivitis urethritis or tenosynovitis there may be carditis chorea, subcutaneous nodules or marginate erythema

If there is no history of recent sore throat or other streptococcal infection evidence of such may be afforded by an anti streptolysin titre in the region of 200 Todd units High titres do not prove that an illness is rheumatic fever, only that there has been recent hæmolytic streptococcal infection Similar proof may be obtained by finding that the patient s serum agglutinates an emulsion of hæmolytic streptococci at a titre of 1 200 It is highly *improbable that any case of acute rheumatic fever, whether it be the first* attack or a recurrence will not show such serological changes

A positive test for C reactive protein in the serum provides good

evidence of activity (Anderson and McCarty 1950) but is far from specific in the rheumatic state the abnormal *alpha* globulin that reacts with C polysaccharide being found in a variety of infections necroses and collagen diseases including uncomplicated streptococcal sore throat rheumatoid arthritis and periarteritis

That continued hæmolytic streptococcal infection is not responsible for the disease may be proved by the lack of improvement after treatment with penicillin

(3) *Response to salicylates* Joint pains and effusions in rheumatic fever commonly respond dramatically to sodium salicylate in initial doses of 15 to 20 grains (1 to 1 5 G) aspirin (or calcium aspirin) 5 to 10 grains (0 3 to 0 6 G) three or four hourly Only the exudative lesion and the associated fever respond no effect is observed on proliferative lesions Sodium salicylate is often used as a diagnostic test but although a good one it is not infallible

(4) *Chorea* Rheumatic or Sydenham s chorea is mysterious in several ways First it has a solitary nature preferring to occur alone rather than in the company of other rheumatic manifestations Secondly it does not affect the sedimentation rate Thirdly there is no specific rheumatic pathology in the brain (Shaw 1929) Nevertheless it is certainly part of the rheumatic state About 20 per cent of patients with chorea alone develop rheumatic heart disease about 50 per cent develop other rheumatic manifestations with or without carditis (Sutton and Dodge 1938) and most of the remainder have a familial link Conversely about 20 per cent of all rheumatic cases have chorea (Ash 1948) Clinical features include spontaneous involuntary inco ordinated movements muscular weakness and alteration of tendon jerks emotional instability and some disturbance of higher cortical function Occasionally it is more or less confined to one side of the body Movements disappear during sleep

The diagnosis of chorea must be made from common tics and other forms of hysteria Reliance should be placed on the quality of the movements They are quick complicated elaborate irregular and varied The same movement is rarely repeated exactly The hands writhe and twist the patient trying to stop them or attempting to conceal them by some volitional act She often drops things she is holding especially crockery or she is clumsy in other ways Facial grimaces are odd and varied unlike the repeated twitch of a tic After protruding the tonge for inspection she withdraws it like a lizard snapping the jaws over it When the hands are held out the wrist is flexed and the fingers hyper extended The knee jerk may be sustained, the leg being held up at the height of its extension for an appreciable interval before relaxation occurs

Hysterical movements are more jerky and show constant repetition Experience and familiarity with both conditions usually makes their distinction easy The involuntary athetotic movements of encephalitis and Wilson s disease may be more confusing

5 *Skin lesions* Petechiæ may occur in the skin or in the fundi in fulminating cases but are in no way specific Petechiæ or purpura may be associated with gut colic and joint pains in the Schonlein Henoch syndrome in these cases acute glomerular nephritis is very common rheumatic carditis rare (5 per cent) The syndrome represents another type of allergic reaction to streptococcal antigen and is related to rheumatic fever nephritis and polyarteritis (Gairdner 1948) Urticaria erythema nodosum and erythema multiforme are sometimes seen, but they too are not specific They are probably allergic skin reactions and when associated with rheumatic fever may depend upon skin sensitisation to the streptococcus or to its toxins Urticaria may be due to a host of antigens erythema nodosum



Fig 9 02 – Erythema marginatum

to the tubercle bacillus the meningococcus or other organisms erythema multiforme is perhaps more closely related to the streptococcus

*Erythema marginatum* (Barlow and Warner 1881) a variety of erythema multiforme is especially important because it is peculiar to the rheumatic state (Cheadle 1889) It appears in rings, crescents ovals or in irregular forms, characterised by a thin red margin outlining a patch of apparently normal skin (fig 9 02) It is distributed chiefly over the trunk and proximal part of the limbs There may be two or three lesions or dozens of them Sometimes the rash is at first composed of irregular erythematous macules (fig 9 03) but the centres soon clear leaving spreading red margins (Perry 1937) Erythema marginatum may be fleeting or remarkably persistent as a rule it is recurrent and may reappear from time to time

long after other manifestations of active rheumatism have subsided It is seen in about 8 per cent of cases in the United Kingdom (joint report 1955)

Subcutaneous nodules occur in one fifth of active cases in this country and are good examples of proliferative rheumatic lesions Like erythema marginatum they were first properly studied by Barlow and Warner (1881) although well recognised long previously (Wells 1810) Varying in size from something so small as to escape clinical detection to the dimension of a Barcelona nut they are usually attached to tendon sheaths to the



Fig 9 03—Erythema multiforme

superficial surface of joint capsules or to other fascia so that the skin rides over them freely They are best seen on the knuckles (fig 9 04a) on the back of the head (fig 9 04b) on the elbows or on the knees In children they are practically diagnostic of rheumatic fever, but similar though usually larger and more persistent nodules may occur in Still s disease and in adult rheumatoid arthritis (Hawthorne 1900) It is doubtful whether there is any fundamental difference between these nodules (Keil 1938) In cases of rheumatic fever nodules have been induced artificially by injecting one of a variety of substances including blood trypsin and hyaluronidase into the fibrous tissue or fascia overlying the olecranon process (Massell Coen and Jones 1950)

6 *Pulmonary signs* Because of its non specific clinical features pleurisy rarely provides evidence of rheumatic fever, but it is not uncommon Paul (1928) gave its incidence as 10 per cent It may be dry or it may give

(a) On the knuckles



(b) On the back of the head

Fig [illegible]04 – Subcutaneous rheumatic nodules.

rise to a sterile straw coloured effusion Response to salicylates is indifferent

Rheumatic pneumonia is rare occurring in only 1 to 2 per cent of active cases Symptoms are not spectacular There is no chill, breathing is not embarrassed the respiratory rate is but little elevated, and fever is not necessarily higher than before Cough may be noted, but is rarely troublesome The sputum is scanty and tenacious occasionally it is streaked with blood Physical signs include dullness to percussion bronchial breathing and crepitations appearing first here then there The transient and migratory nature of these signs is characteristic Serial skiagrams confirm the presence of patchy wandering consolidation or may show a variable broncho pneumonic pattern (fig 905) The white blood count is little altered Rheumatic pneumonia is not influenced by penicillin sulphonamides or salicylates fortunately it does not often appear to alter the course of the major illness

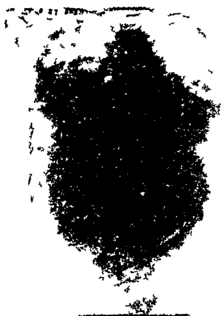


Fig 905—Skiagram showing rheumatic pneumonia in a girl

Most cases studied at autopsy have been unusually severe and consolidation has been extensive and mostly lobar in distribution The affected parts are bulky have a peculiar succulent gelatinous appearance (Hadfield 1938) and feel like indiarubber in colour they are a homogenous rich purplish red (Naish 1928 Eiman and Gouley 1928) and later may be buff Microscopically the predominant finding is an extensive fibrinous exudate infiltrated with mononuclear and multinucleated cells Polymorphs and lymphocytes are scanty The cellular exudate is partly interstitial but also line the alveolar ducts and may fill the alveoli (Hadfield 1938) There is associated hyperæmia and œdema Secondary fibroblastic reaction develops later, and when interstitial may be responsible for pulmonary hypertension (Gouley 1938) Similar lesions have been produced experimentally by Rich and Gregory (1943)

Simple collapse of either lower lobe in the course of rheumatic fever may occur, and must not be confused with rheumatic pneumonia Its cause is obscure, but it may be connected with the long recumbent posture It is seen in many serious illnesses that confine a patient to bed for a long time e g typhoid fever Sometimes collapse of the left lower lobe may be

due to pericardial effusion or to a greatly dilated heart Pulmonary congestion or œdema and infarcts of the lung should be recognised without difficulty

7 *Tolerance to Heparin* Patients with acute rheumatic fever show a remarkable tolerance to heparin and possibly to other sulphated polysaccharides This is at present under investigation and may prove a useful test for the active rheumatic state (Abrahams and Glynn 1949)

## EVIDENCE OF CARDITIS

To establish the diagnosis of rheumatic carditis at least one of its five chief manifestations must be recognised It should be clearly understood that while these offer proof of cardiac involvement they do not by themselves necessarily signify a rheumatic etiology—that must be demonstrated in other ways

1 *Mitral valvitis*

1 The development of a *mitral pan systolic murmur* embracing both heart sounds at the apical area must be taken seriously Towards the end of the nineteenth century apical systolic murmurs of all kinds were attributed to mitral valve disease and patients were put to bed for long periods unnecessarily to combat this tendency Mackenzie taught that the apical systolic murmur could be safely disregarded when unaccompanied by other signs of heart disease and this teaching was perpetuated and emphasised by Lewis and Parkinson As a result the original diagnostic fault *has been over corrected and it is becoming increasingly obvious that an* important murmur is not receiving proper attention The confusion has been caused partly by *failure to distinguish the pan systolic murmur of* mitral incompetence from the relatively short mid systolic aortic ejection murmur transmitted to the apex The latter is often innocent as explained elsewhere but the mitral pan systolic murmur means mitral incompetence and nothing else and it is high time this indisputable fact was more widely recognised The mitral murmur of course must be distinguished from the pan systolic murmur of ventricular septal defect and tricuspid incompetence both of which may be heard best sometimes at the apex of the heart but if the apical murmur is mitral then the only diagnostic problem is whether the mitral incompetence is functional secondary to ring dilatation or organic resulting from a diseased mitral valve Functional mitral incompetence means left ventricular dilatation just as functional tricuspid incompetence means right ventricular dilatation and both are important for dilatation of either ventricle cannot be viewed with equanimity In rheumatic carditis for example functional mitral incompetence usually means serious aortic incompetence with or without left ventricular failure and is far more important than trivial mitral valvulitis to which an isolated mitral pan systolic murmur should be ordinarily attributed

In quality the mitral pan systolic murmur is usually loud smooth and blowing being of fairly high frequency it is better heard with the diaphragm type of chest piece A thrill is uncommon in the early stage of active inflammation and when it occurs usually means considerable permanent damage to the valve Follow up studies have shown that chronic rheumatic heart disease develops in 45 per cent of cases in which the original murmur was loud and in only 9 per cent of those in which it was soft (Boone and Levine 1938 Kuttner and Markowitz 1948)

*Other evidence of significant mitral incompetence* includes a small slightly water hammer pulse, an otherwise unexplained rise of venous pressure a hyperdynamic enlarged left ventricle (clinically electrocardiographically and radiologically) a loud third heart sound and radiological evidence of dilatation of the left atrium with or without pulmonary venous congestion When valvitis is severe, permanent incompetence may be established within a few weeks of the onset of rheumatic carditis

The development of a *soft short mitral diastolic murmur* (Carey Coombs murmur) in the absence of any other sign of mitral stenosis provides by far the most useful and conclusive evidence of mitral valvitis At the rheumatic fever centre Taplow this murmur has been heard in 75 to 80 per cent of active cases Although transient in 20 to 25 per cent it usually proves to be more or less persistent or reappears on the least provocation until pre systolic accentuation and a loud first heart sound proclaim the development of mitral stenosis (Carey Coombs 1924)

This characteristic and diagnostic murmur is frequently overlooked because it is very low pitched soft and short it is best heard with the bell stethoscope when the patient lies on the left side especially as the heart slows down after effort and has the typical mid diastolic timing of all mitral diastolic murmurs We thought at Taplow that the murmur could be brought out or accentuated by any agent that increased the mitral stroke blood flow and that phenylephrine (neosynephrine) was perhaps the best way of achieving this When given in doses of 0 25 mg intravenously the blood pressure rises sharply and the murmur develops as the heart slows down (Besterman 1951)

Necropsies have confirmed the fact that this murmur may occur in active rheumatic carditis when the mitral valve is scarcely altered (Bland White and Jones 1935) It has therefore been suggested that its mechanism depends upon left ventricular dilatation that it is related to the Austin Flint murmur and to the soft mitral diastolic murmur that is occasionally heard in thyrotoxic heart failure But it must be pointed out that the Carey Coombs murmur is usually heard when no enlargement of the heart can be demonstrated and it is more reasonable to believe that some change in the structure of the mitral valve is responsible Whatever the explanation there is no doubt that this murmur occurs early in the course of rheumatic carditis and may disappear as activity subsides

2 *Aortic valvitis*

Inflammation of the aortic valve usually leads to immediate and permanent aortic incompetence which may be recognised at once by the tell tale *aortic diastolic murmur* The initial leak is small so that other evidence is usually lacking When first heard the murmur may be remarkably short and high pitched and its onset is slightly delayed being *inaudible* until the diastolic pressure gradient across the aortic valve is approaching its maximum i e towards the end of the period of isometric relaxation when the left ventricular pressure is approaching zero The triple rhythm cadence so produced may be disconcerting to the student who is only familiar with the to and fro murmurs of well established aortic valve disease but it is characteristic of these early cases

An aortic diastolic murmur was heard in 35 per cent of cases at Taplow and one in five was transient Phenylephrine was again helpful in accentuating the murmur or bringing it out when it could not otherwise be heard for the temporarily raised blood pressure and increased stroke volume encouraged the leak (Besterman 1951)

An *isolated aortic mid systolic ejection murmur* heard best at apex or base provides insufficient evidence of aortic valvitis to warrant a diagnosis of active rheumatic carditis for it is too commonly produced by a simple increase of blood flow associated with any fever or as a result of other innocent phenomena such as a depressed sternum A functional basal systolic bruit may also be pulmonary rather than aortic and this too is usually a functional flow murmur turbulence being created by a variety of innocent causes

3 *Partial heart block*

Transient prolongation of the P R interval (fig 9 06) is recorded in about 10 per cent of cases but may well be more frequent than this It may be recognised clinically by premature *a* waves in the jugular venous pulse occasionally by regular venous cannon waves *when P falls between the onset* of QRS and the end of the T wave of the previous cycle, by premature pre systolic gallop rhythm the interval between pre systolic and first heart sounds being prolonged and by *softening of the* first heart sound the atrioventricular valve cusps floating into apposition after atrial contraction is completed so that the atrioventricular valves are already more or less




Fig 9 06—Electrocardiogram showing prolongation of the P R interval in a case of active rheumatic carditis

closed when the ventricles contract Dropped beats are unusual and more severe grades of heart block rare Normal conduction can be temporarily restored in 90 per cent of cases by means of 1 to 2 mg of atropine sulphate intravenously (Bruenn, 1937) Some degree of permanent block is likely in those that do not respond to atropine

4 *Pericarditis*

Rheumatic pericarditis occurs in about 10 per cent of cases it is always acute commonly develops during the first month of the illness and leaves no clinical sequelæ In mild cases there is little more than transient pericardial friction with or without pain Most cases that are recognised however are relatively severe and the inflammation is accompanied by considerable pain high fever rapid breathing and obvious distress there is usually leucocytosis and the sedimentation rate is always high A rise of venous pressure and proportionate distension of the liver are usual, for fluid tends to accumulate rapidly dangerous tamponade however is rare and therapeutic tapping nearly always unnecessary The electrocardiogram may show characteristic early elevation of the S T segment followed by flattening or slight inversion of the T waves in most leads as in other forms of pericarditis (fig 9 07) but these changes are found in only a little over half the cases and are rarely very conspicuous Rapid changes in the size of the heart shadow provide the most reliable radiological evidence of pericardial effusion (fig 9 08) changes in shape being less important Samples of the fluid are straw coloured, sterile and have the physical properties of an exudate

Pericardial effusion is the usual cause of apparent cardiac enlargement in rheumatic carditis in the absence of serious valve damage or heart failure (Wood 1950 Thomas Besterman and Hollman 1953)

5 *Heart failure*

Investigations on cardiac function in rheumatic carditis carried out at Taplow seemed to establish three things (1) in cases uncomplicated by gross valve damage pericardial effusion or congestive heart failure tachycardia is not disproportionate to fever and anxiety and the relationship between cardiac output and heart rate does not differ from that in normal controls (Hoffman 1950) (2) cardiac dilatation rarely if ever occurs in simple rheumatic carditis enlargement of the heart shadow nearly always being caused by serious permanent valve damage, pericardial effusion or congestive failure (Wood 1950 Besterman and Thomas 1953) (3) the resting cardiac output in uncomplicated cases is probably normal but the maximum output is strictly limited and frequently reached as a result of anxiety alone (Besterman 1954) There is no simple bedside way of demonstrating this impairment of cardiac function

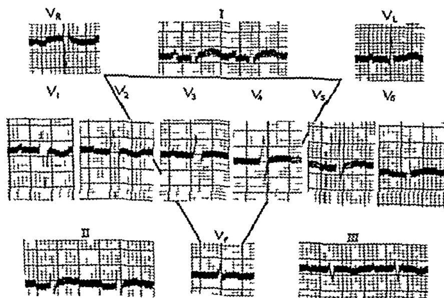
Congestive heart failure proper with elevation of the venous pressure distension of the liver and a fall in cardiac output, with or without œdema or ascites is rare in the absence of advanced aortic or mitral valve disease

$V_R$ I $V_L$

$V_1$ $V_2$ $V_3$ $V_4$ $V_5$ $V_6$

II $V_F$ III

(a) Early stage with elevation of the S T segment




(b) Three days later with flattened T waves

Fig. 10.—The electrocardiogram in rheumatic pericarditis



(a) 24th November 1947 (b) 1st December 1947

Fig 9 08—Rapid change in the size of the heart shadow in a case of pericardial effusion

its development during the course of rheumatic fever provides good evidence of active carditis

The chief clinical difficulty is to distinguish heart failure from pericardial effusion The points favouring effusion have already been enumerated *The distinguishing features of heart failure include (1) the relatively late* onset of the episode in question the signs suggesting heart failure rarely appearing within the first three months of the illness (2) the presence of advanced aortic or mitral valve disease usually incompetence (3) a low or falling sedimentation rate absence of leucocytosis and a normal or subnormal temperature (4) œdema or ascites (5) a relatively fixed degree of cardiac enlargement (6) radiological evidence of pulmonary venous congestion but no pleural effusion (7) a good response to digitalis therapy (Thomas 1954)

Despite these numerous points of difference the distinction between acute pericarditis with effusion and heart failure may be difficult at times Figure 9 09, for example illustrates the rapid development of cardiac dilatation from heart failure The first skiagram (a) was taken on the 23rd March 1948 in a quiescent phase one week before a recurrence of rheumatic fever at a time when the temperature was normal the E S R 18 and the only evidence of carditis a Carey Coombs murmur The second skiagram (b) was obtained six weeks later on the 8th May one week before death, and shows gross dilatation of the heart shadow at a time when the patient s temperature was 102 degrees F the sedimentation rate 56 and pericardial friction widespread At necropsy there was only 20 ml of fluid



(a) 23rd March 1948 (b) 8th May 1948

Fig 9 09—Unusually rapid change in the size of the heart shadow in a case of heart failure (see text)

in the pericardial sac and the enlargement was caused chiefly by dilatation of the left ventricle as a result of heart failure secondary to rheumatic carditis in the presence of advanced aortic and mitral valve disease The pericardium however was considerably thickened

The only way we were able to establish the criteria for distinguishing between cardiac dilatation and pericardial effusion was by proving which was present by means of cardiac catheterisation (fig 4 57)

*Other manifestations of carditis*

It is doubted if there are any other manifestations of rheumatic carditis *Sinus tachycardia* is not disproportionate to fever anxiety pericardial effusion or heart failure *Gallop rhythm* in a child is difficult to distinguish from a normal third heart sound *Enlargement of the heart shadow* rarely if ever occurs in the absence of advanced valve disease heart failure or pericardial effusion

The *electrocardiogram* shows no obvious changes other than those depicting partial heart block pericarditis or the consequences of advanced valve disease

Prolongation of the Q T interval was found by Taran and Szilagyi (1947) in practically all cases of active carditis and this has been confirmed apparently by Abrahams (1949) In fig 9 10 the corrected Q T interval (QT ) in sixty cases of active carditis and fourteen cases of rheumatic fever without carditis has been plotted against the sedimentation rate on a semi logarithmic scale It will be seen that about 90 per cent of those with

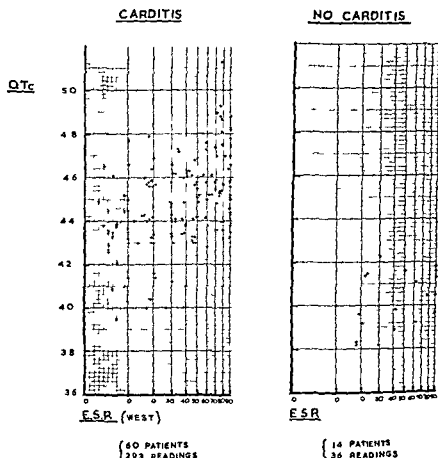



*Fig 9 10—Graph showing QT plotted against the sedimentation rate in 60 ca es of active rheumatic carditis and in 14 rheumatic fever controls without carditis*
*(By ou t y f D D k Ab ah t s)*

carditis have a QT longer than 0 42 second whereas all but one of those without carditis fall below this level Fig 9 11 shows the behaviour of QT in six typical cases of acute rheumatic carditis with rapid recovery In fig 9 12 a relapse is portrayed it may be observed that QT then remains grossly prolonged although the sedimentation rate is falling towards normal If the long $QT_c$ is ignored and the patient is allowed up relapse may occur It must be stated however that further detailed work on the behaviour of $QT_c$ in rheumatic carditis has thrown considerable doubt on its value

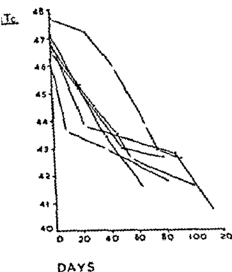



Fig 9 11—Behaviour of QT in six cases of acute rheumatic carditis with rapid clinical recovery

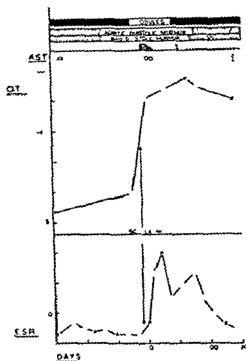



Fig 9 12—Prolonged QT following a recurrence of active rheumatic carditis

(By courtesy of Dr Derek Abrahams)

## TREATMENT

All cases of acute or subacute rheumatic polyarthritis should be put to bed and treated with sodium salicylate, 15 to 20 grains (1 to 1 5 G), combined or not with twice as much sodium bicarbonate three hourly (Lees 1904) until relieved or until ringing in the ears and deafness proclaim that the desired therapeutic salicylate blood level of 30 to 35 mg per cent has been reached when the interval between doses may be increased to four or six hours Aspirin or calcium aspirin, 10 gr (0.6 G), is equally effective Fever pain and joint effusions usually subside quickly but proliferative lesions including carditis are resistant Toxic effects are minimised by alkalis this has been attributed to an increased rate of salicylate excretion in their presence (Parker 1947 1948) Toxic effects include central vomiting hyperventilation associated with an increased oxygen consumption (Cochran 1952) and which sometimes results in reduction of the plasma $CO_2$ content (Graham and Parker 1948) and petechiæ associated with prolongation of the prothrombin time (Link *et al*, 1943) Fatal hæmorrhagic encephalopathy has been reported (Ashworth

and Mckenzie, 1944) *Circulating prothrombin can usually be restored by means of vitamin K in doses of 10 to 50 mg* (Shapiro 1944)

When the patient has been free from symptoms for a week or if he fails to derive benefit salicylates should be stopped If clinical relapse follows no harm is done for the exudative lesion is relatively innocent, and is soon controlled by another course

Salicylates were introduced by Bliss (1875) and Maclagan (1876) and their action is still uncertain It was suggested long ago that they might *inhibit antibody formation* (Derick Hitchcock and Swift 1927–8) a con *ception that received some support from* Jager and Nickerson (1947) who showed that salicylates reduced the amount of H and O antigens produced in response to typhoid vaccine Salicylates increase the plasma volume (York and Fischer 1947) there being a profound shift in the distribution of body fluid from intracellular to extracellular compartments (Reid Watson and Sproull 1950) Following this line of thought Copeman and Pugh (1950) reported rapid clinical improvement in 7 cases of acute rheumatic fever following an injection of hypertonic saline the patients having been dehydrated previously by means of food and fluid starvation for 36 hours *Another way in which salicylates may influence the symptoms* of rheumatic fever is by inhibiting hyaluronidase (Guerra 1946) This enzyme hydrolyses hyaluronic acid a polysaccharide present in muco protein which is a constituent of the ground substance of all connective tissue (Chain and Duthie 1939) The effect of this is to increase the rapidity with which substances spread through collagen as may be demon strated by measuring the rate of spread of a suitable dye when injected intradermally *In rheumatic fever injected dye spreads more rapidly than in normal controls as if an excess of* hyaluronidase were *present* (Guerra 1946) and serum from patients with active rheumatic fever has been shown to contain an excess of anti hyaluronidase (Quinn 1948) Whether the hyaluronidase factor in rheumatic fever depends on the power of the culpable streptococcus to produce it or whether it arises from some other source is immaterial in respect of the action of salicylates, although possibly fundamental in relation to the cause of rheumatic fever *itself* *Another effect of salicylates is to reduce the permeability of damaged* capillaries (Swyer 1948) and *this should certainly* limit the exudative reaction Yet another hypothesis is that salicylates have an action like A C T H for Hetzel and Hine (1951) have shown that therapeutic doses of salicylates diminish the ascorbic acid content of the suprarenal glands in rats (generally regarded as evidence of increased cortical activity) *the* effect being abolished by hypophysectomy Van Cauwenberge (1951) found a reduction *of circulating* eosinophils in rats *four to six hours after the ingestion of salicylates* preceded by a significant *increase* of the urinary *uric* acid/creatinine ratio both of which have been attributed to increased activity of the suprarenal cortex Finally, it must be remembered that a break down product of sodium salicylate may well be responsible for its

therapeutic effects rather than the drug itself and in gentisic acid we have a metabolite that seems to fulfil these expectations sodium gentisate in doses of 1 G three hourly relieves the symptoms of rheumatic fever as quickly and completely as salicylates and has the advantage of minimal toxic effects (Meyer and Ragan 1948 Clarke 1953)

Recent work at the Mayo Clinic on the beneficial effect of cortisone (17 hydroxy 11 dehydrocorticosterone) on rheumatoid arthritis (Hench *et al* 1949) provided a new approach to the treatment of rheumatic states in general but initial enthusiasm has already abated and in rheumatic fever both cortisone and A C T H have been shown to be no more effective than aspirin (joint report 1955) The usual dose of cortisone is 200 mg daily for the first week 100 mg daily for the second and third weeks and 75 to 25 mg thereafter the daily dose being reduced by 25 mg at weekly intervals and the total course lasting six weeks Cortisone may be given intramuscularly or by mouth A C T H (adreno cortico trophic hormone or corticotropin) is given intramuscularly in daily doses of 100 units for the first week 80 units for the second 60 units for the third 40 for the fourth 30 for the fifth and 20 for the sixth

Both cortisone and corticotropin like aspirin relieve fever and joint pains quickly in rheumatic fever and the sedimentation rate falls in a gratifying manner but myocarditis endocarditis pericarditis nodules erythema marginatum and chorea do not seem to be influenced by any of these substances

Neither sulphonamides nor penicillin have any influence on the course of rheumatic fever if given after the onset of rheumatic symptoms but both are valuable prophylactic agents Sulphadiazine in doses of 0 5 G once or twice daily oral penicillin or benzathine penicillin in doses of 200 000 to 500 000 units daily or monthly intramuscular injections of 1 2 to 1 5 mega units of benzathine penicillin, all greatly reduce the frequency with which group A hæmolytic streptococci can be cultured from the throats of rheumatic children or carriers and reduce the frequency of recurrences (Stollerman Rusoff and Hirschfeld 1954 Perry and Gillespie 1954) Unfortunately intramuscular benzathine penicillin is often very painful There is also good evidence that penicillin lessens the chances of the rheumatic reaction if given early enough to cases of group A hæmolytic streptococcal sore throat (Rammelkamp 1952) and this may be supported by the demonstration that penicillin therapy suppresses antibody formation as judged by the anti streptolysin titre and that the sooner penicillin is given in cases of tonsillitis the greater the suppression of antibody (Brock and Siegel 1953)

*Tonsillectomy* is only necessary if there is chronic sepsis or if there is recurrent tonsillitis it has little influence on the disease and does not prevent relapse or recurrence (Ash 1938) A good nourishing diet fresh air vitamins especially vitamin C appropriate treatment of secondary anæmia and high morale are more important

Chorea usually lasts 6 to 12 weeks Patients should be put to bed during the active phase, and may need heavy sedation If there is no evidence of carditis they may be allowed up when recovery begins They should be kept away from school and from social engagements until well

Carditis requires absolute rest Little else is of lasting value Digitalis is helpful when there is congestive heart failure and although the thera peutic dose is said to be close to the toxic ill effects have not been observed at Taplow Mercurial diuretics and a low sodium diet are rarely necessary

Absolute rest means that the patient is allowed to do nothing for himself he is washed and fed and must use bed pan and urine bottle Diet should be light and constipation avoided In the past it was usual to insist on nursing the patient in the horizontal position with one low pillow but it is clear from experience gained in the treatment of angina decubitus and of paroxysmal cardiac dyspnœa and from certain direct investigations in man that the cardiac output and therefore the work of the heart, is greater in the horizontal than in the upright position owing to the influence of gravity on the venous filling pressure It is therefore logical *to nurse* patients with carditis in the sitting posture The wisest course may be to chose the position of maximum comfort whether lying or sitting unless there is failure when the latter should be insisted upon

By far the best index of activity is the E S R , which should be measured weekly and as a rule the patient should not be allowed up until it is normal This applies especially to children in whom carditis should be assumed *for purposes of early management* Adults without evidence of previous or pre sent carditis may be treated more leniently and may be allowed up as soon as they appear well enough on clinical grounds The duration of bed rest varies between a week or two and several months according to the severity and persistence of the active process If patients are allowed up too soon swift relapse is the rule

Convalescence from carditis should be extended over several months the regime being similar to that for pulmonary tuberculosis Relapse is common and may be due to over exertion exposure, emotional upset, cold damp weather, and to almost any infection Relapse follows the advent of the responsible agent immediately and must be distinguished from a recur *rence or second attack of rheumatic fever in which streptococcal infection* is always to blame and following which a latent interval can usually be recognised At least one recurrence occurs in two thirds of all cases usually within three years (Roth Lingg and Whittemore 1937)

It is as important to prevent cardiac neurosis in patients with organic heart disease as it is in those without This is a difficult task in susceptible individuals for reassurance cannot very well be unconditional Rheumatic carditis may be symptom free and pass without influencing the subject's activities at all Thus only about 55 per cent of cases of mitral stenosis give a history of the original attack (Parkinson and Hartley 1946) Many others are only restricted by subacute rheumatism Little immediate harm comes

to these patients indeed there is no direct evidence that subsequent development of mitral stenosis could have been prevented by bed rest at the time of active inflammation It follows that failure to diagnose carditis when it is present in rheumatic fever is not necessarily disastrous On the other hand its diagnosis in error may not be far short of it for the resulting cardiac neurosis which is so common may be life long and may be more incapacitating than organic heart disease Physicians should be more aware of their responsibility in this respect Too much emphasis is laid on over looking a mild lesion not enough on finding what is not there The most common mistake is to misinterpret tachycardia A patient confined strictly to bed for several weeks with rheumatic fever is fully aware that his heart may be involved and is likely to become nervous on that account Tachycardia may then be due to anxiety Again, the autonomic nervous system is frequently disturbed by fever and infections of all kinds tachycardia dizziness, headache and fatigue may result especially during convalescence when activities are re umed Such findings call for reassurance and rehabilitation not for alarm and further rest

*In the absence* of diagnostic evidence of carditis throughout the active phase of rheumatic fever subsequent medical management should be based on the assumption that none existed not upon the fear that it escaped recognition and patients should be sent for convalescence as after any other fever of equal severity This attitude is based not on the belief that carditis does not occur in a certain percentage of children with rheumatic fever but on the fact that if it does occur in an indetectable degree it is *either of no consequence or it is not aggravated by* this kind of management and on the fact that the over cautious attitude breeds neurosis

## COURSE AND PROGNOSIS

Following convalescence from rheumatic fever between 60 and 65 per cent of cases have evidence of residual valve damage but 10 to 20 years later 9 to 16 per cent of these seem to have *recovered completely on the* other hand 23 to 44 per cent of those who appear to escape unscathed *develop signs of chronic* rheumatic heart disease within the same 10 to 20 year period (Ash 1948 Bland and Jones 1951) The net result is that at least two thirds of all cases of rheumatic fever in childhood develop permanent valve damage.

Rheumatic carditis is more likely to be associated with polyarthritis (61 per cent) than with subacute rheumatism (38 per cent) or chorea (20 per cent) Isolated carditis however must occur much more frequently *than its 15 per cent incidence would imply* because 40 per cent of all cases of chronic rheumatic heart disease in adults give no history of any rheumatic manifestations in childhood Allowing for this it is estimated that one third of all rheumatic cases in childhood have isolated carditis and that two thirds of these are overlooked at the time No previously published

figures concerning early mortality and ultimate prognosis have allowed for these silent cases of primary carditis For example according to Ash (1948) about 48 per cent of cases presenting with primary carditis in childhood die within 10 years but these of course are the cases that are recognised because of their severity and isolated rheumatic carditis must be severe to cause symptoms If allowance is made for the relatively mild unrecognised cases practically none of which die within 10 years Ash s figure changes from 48 to 16 per cent

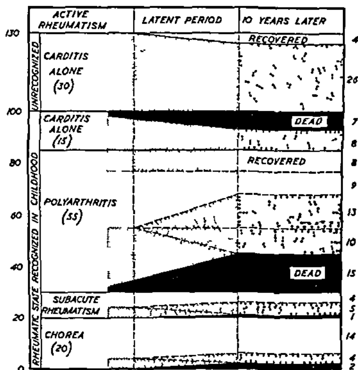
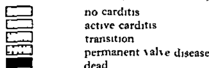



Fig 9 13—Chart depicting the course of the rheumatic state over the first ten years (modified from figures published by Rachel Ash 1948)




In figure 9 13 an attempt has been made to chart the course of rheumatic fever over the first 10 years based on the papers by Ash (1948) and Bland and Jones (1951) but modified so as to allow for the unrecognised cases Taking into consideration the known data it may be calculated that to every 100 recognised cases of juvenile rheumatism with or without carditis there must be an additional 30 cases of unrecognised pure rheumatic carditis assuming that between 10 and 15 per cent of the latter recover

completely as in the recognised cases of carditis The chart shows that 10 years after the onset of the rheumatic state 25 out of 130 cases are dead (19 per cent) 66 (51 per cent) have chronic rheumatic heart disease and 39 have recovered completely (30 per cent) It also shows that of the 66 living cases with permanent valve damage 26 (40 per cent) were not recognised during the stage of active carditis The relatively good prognosis of subacute rheumatism and chorea will not escape notice

Of the fatal cases one third die within one year of the onset of rheumatic carditis and two thirds (Bland and Jones 1938) to three quarters (Ash 1948) within the first five years Thus the immediate mortality is 6 5 per cent as reported by Scott (1943) Sudden unexpected death is rare in contrast to its frequency in diphtheritic and certain other forms of toxic myocarditis thus there were only three such instances amongst a group of 7 165 cases of active rheumatic fever reported by Griffith and Huntington (1946) coronary angiitis was blamed

The prognosis is of course greatly influenced by the severity of the active state Thus in a 20 year follow up study of 1 000 cases Bland and Jones (1951) found that 80 per cent of those who had developed heart failure 63 per cent of those with pericarditis and 37 per cent of those with nodules had died

Recurrences or relapses are the rule rather than the exception 40 per cent of cases having a second attack within 2 years 58 per cent within 5 years and 63 per cent within 10 years (Ash, 1948) Thus two thirds of recurrences might be prevented by adequate antibiotic therapy for a period of two years after the initial attack

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CHAPTER X

# CHRONIC RHEUMATIC HEART DISEASE

RHEUMATIC carditis refers to active inflammation of the heart The after effects which include valve sclerosis patchy myocardial fibrosis, and adherent pericardium are best described under the general heading of rheumatic heart disease to which the appropriate anatomical abnormality may be appended Thus we may speak of rheumatic heart disease with mitral stenosis

About 5 per cent of healthy young adults give a previous history of rheumatic fever in childhood (Parkinson and Hartley 1946) It is clear therefore that all patients who have rheumatic fever do not later develop clinical rheumatic heart disease According to Carey Coombs (1924) 50 per cent of children who have their first attack of rheumatic fever before they are five years old and 25 per cent of those whose first attack occurs after the age of ten subsequently develop rheumatic heart disease As described in the last chapter recent studies indicate that more accurate figures for these two groups would be 75 and 50 per cent respectively The frequency of permanent valve damage from primary rheumatic fever after the age of 20 does not seem to be known but is far from negligible

From large samples of the younger male population of Great Britain examined for military service between 1939 and 1945 it was calculated that there were about 240 000 cases of rheumatic heart disease of both sexes between the ages of 18 and 44 in Great Britain at that time or about 2 6 per cent of the population in that age group (Parkinson 1945) Rheumatic heart disease accounts for approximately 20 per cent of all cases of heart disease in temperate climates and causes about 10 000 deaths annually in Great Britain

Practically all clinical cases of inactive rheumatic heart disease have one or more valve lesions The mitral valve is involved in 85 per cent, the aortic in 44 per cent the tricuspid in 10 to 16 per cent, and the pulmonary in 1 to 2 per cent (Cabot 1926) The relative frequency with which each valve is affected is proportional to the pressure load against which each normally operates

The rheumatic process affects the heart muscle as well as the valves and this may result in a varying degree of permanent interstitial myocardial fibrosis. Moreover, it has long been known that careful microscopy reveals Aschoff nodes in all stages of development maturity and senescence in about 50 per cent of all fatal cases of chronic rheumatic heart disease the figure being higher in those that die under the age of 40 years than in older patients (de la Chapelle Graefe and Rottino 1934 Werner 1936)

The more recent frequent discovery of Aschoff nodes in left atrial appendicular biopsies in 45 to 50 per cent of cases of mitral stenosis treated by valvotomy (Decker *et al* 1953 McKeown 1953) should have caused no surprise and merely confirms what was already well established Although there is usually no other pathological or clinical evidence of activity in these cases there is no valid reason for doubting that these Aschoff nodes represent continually relapsing or chronic active carditis Although the myocardial lesion is certainly less important than the valve damage in at least 95 per cent of cases it cannot be ignored

Rheumatic pericarditis leaves no clinical sequelæ Although the pericardium may become adherent to surrounding structures or its two layers fused and thickened such changes do not seem to interfere with cardiac function Chronic constrictive pericarditis is never rheumatic For the most part then chronic rheumatic heart disease is mitral aortic or tricuspid valve disease or any combination of these three lesions together with their complications its course may be modified but very rarely determined by relapsing or chronic myocarditis or by the degree of myocardial fibrosis present

## MITRAL INCOMPETENCE

In the last century this was the most common valve lesion diagnosed Owing to the exertions of Mackenzie Lewis Parkinson and others the first half of the twentieth century witnessed a diagnostic revolution so that a physician who asserted that a patient had organic mitral incompetence had to be very sure of his grounds The change in outlook saved a host of normal subjects from invalidism But the pendulum swung much too far and serious efforts were being made to correct this tendency when the introduction of mitral valve surgery in 1948 forced the pace so that in a short space of time the whole subject received the concentrated attention of investigators all over the world and mitral incompetence was quickly seen in its proper perspective

### *INCIDENCE*

In an unselected series of 300 cases of mitral valve disease studied in detail by the author mitral incompetence was the major hæmodynamic fault in 34 per cent (Wood 1954) About half of these cases had no obstructive stenosis and the other half had mixed stenosis and incompetence with the latter dominant *Mild incompetence complicating* dominant stenosis will be considered later This means that in rheumatic heart disease mitral incompetence is the main valve lesion more often than aortic stenosis or aortic incompetence but not as often as aortic valve disease as a whole Approximately 70 per cent of the cases were serious and would have been treated surgically had there been a satisfactory valve repair operation to offer

## AGE AND SEX

The average age of the patients with mitral incompetence was 37 2 which was the same as the average age of the patients with mitral stenosis

The sex ratio is 3 2 in favour of males in cases of pure mitral incompetence and 1 1 in mixed cases in which incompetence is at least as important as the stenosis

## PATHOLOGY

As emphasised by Brock (1952) serious mitral incompetence means greater disorganisation of the mitral valve mechanism than that found in simple mitral stenosis and implies a more vicious form of active endocarditis in the first instance a view supported by the previous history actually obtained (Wood 1954)

The most important causes of mitral incompetence are shortening of the valve cusps so that they cannot meet in systole and shortening of the musculo tendinous control the papillary muscles and chordæ tendinæ being shortened matted and densely adherent to the valve so that the latter cannot close Brock (1952) graphically described the situation as a fibrous ankylosis of the valve mechanism the two chief causes cited being commonly found together Heavy calcification is not infrequently associated and adds to the rigidity of the system although its very exuberance may diminish the size of the orifice

Mitral ring dilatation is a relatively rare cause of incompetence in chronic rheumatic heart disease in these cases the orifice is very large and although the cusps may be short and thick there is less fibrous rigidity than in the type previously described Early left ventricular failure with ring dilatation during the stage of active carditis may be responsible

## HÆMODYNAMICS

During systolic the blood that leaks back into the left atrium increases the volume of that chamber and the pressure within it When the left ventricle relaxes in diastole it is subjected to the high filling pressure built up in the left atrium during systole and since there is no real obstruction at the mitral orifice it fills rapidly and dilates to accommodate the extra blood that leaked back during the previous cycle The stroke volume of the left ventricle is therefore increased by the amount of regurgitant blood forward flow being maintained as near to normal as possible although falling short of the ideal in all serious cases In the majority of cases with fibrous ankylosis of the mitral valve left ventricular dilatation is unlikely to exert any influence on the mitral ring or size of the orifice a vicious circle mechanism however is easily established in active rheumatic carditis and in functional mitral incompetence secondary to left ventricular failure from other causes

Although the left atrial pressure may be very high during ventricular

systole, it falls quickly to ventricular level in diastole so that mean left atrial and pulmonary artery pressures are lower than in mitral stenosis of comparable severity Short of left ventricular failure the patient with mitral incompetence is also less embarrassed by tachycardia or sudden increases of right ventricular output than his sister with mitral stenosis for a shortened diastole does not prevent proper ventricular filling and the hyperdynamic left ventricle may have sufficient reserve to deal with an increased flow Moreover, peripheral vasodilatation on effort encourages forward flow

The pulmonary vascular resistance may rise moderately in severe mitral incompetence but rarely reaches extreme levels probably because passive pulmonary hypertension is rarely high enough to excite a vasoconstrictor response

## CLINICAL FEATURES

### *Life history*

Organic mitral incompetence severe enough to shape the medical destiny of the patient is usually well established during the stage of active carditis unlike mitral stenosis its detection demands no latent interval Subsequent sclerosis of valve cusps and chordæ may modify the leak but as a rule there is little basic change in the physiology of the situation over the years until left ventricular failure sets in or reactive pulmonary hypertension alters the course of events The date of the initial inflammation and the average age of death are much the same as in mitral stenosis (q v ) but the symptom free period is a little longer and the downhill course once symptoms have started is a little quicker in mitral incompetence (5 3 years to reach total incapacity against 7 3 years in mitral stenosis)

### *Symptoms*

The symptoms of pure mitral incompetence are usually less spectacular than those of mitral stenosis *Acute pulmonary œdema, for example* is eight times less common, presumably because the mean left atrial pressure is rarely so high as in mitral stenosis of comparable severity and does not rise so sharply on effort or as a result of tachycardia Hæmoptysis is half as common as in mitral stenosis no doubt for the same reason *Angina pectoris is also only half as common despite the increased work undertaken by the left ventricle this may be attributed to the rarity of an extreme pul*monary vascular resistance so that forward flow and therefore coronary filling are not hindered by this additional factor Systemic embolism is at least one and a half times less frequent than in mitral stenosis probably because there is less stasis in the left atrium

In mixed cases in which it is uncertain whether stenosis or incompetence is dominant even after elaborate investigation and even digital examination of the valve both hæmoptysis and systemic embolism are at least as common as they are in mitral stenosis perhaps more so The mean left atrial

pressure is higher in these cases then in pure incompetence and there is more stasis to encourage thrombosis in the conspicuously dilated left atrium

According to Brigden and Leatham (1953) the only special symptom of mitral incompetence is palpitation and they ascribe this to the frequency of ectopic beats The hyperdynamic action of the left ventricle, however may also contribute to this symptom

Effort intolerance is usually due to dyspnœa caused by pulmonary venous congestion as in mitral stenosis but sooner or later left ventricular failure adds its own contribution Some protection may be afforded by the rapid dilatation of the left ventricle early in diastole so that the inter ventricular septum bulges into the cavity of the right ventricle, and interferes with proper filling of that chamber (Bernheim effect) Congestive failure usually occurs without a high pulmonary vascular resistance the œdema being due to the poor renal blood flow secondary to the low output, and the raised venous pressure partly to hydræmia and perhaps partly to a Bernheim effect The left ventricle is certainly over loaded but the right may very well not be This behaviour is radically different from the congestive failure of mitral stenosis for which a high pulmonary vascular resistance or uncontrolled atrial fibrillation is nearly always chiefly responsible

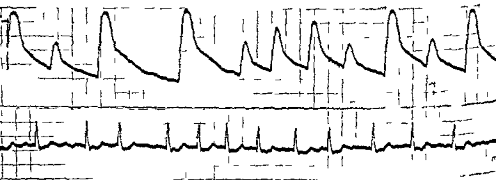


Fig 10 01 —Direct brachial arteriogram from a case of mitral incompetence showing an abrupt percussion wave ill sustained peak and late systolic collapse

*Physical signs*

The patient is usually a man and may look well Peripheral cyanosis may be seen in mixed cases of stenosis and incompetence with a high pulmonary vascular resistance but is rare with pure incompetence

The *peripheral pulse* is small and often slightly water hammer in quality for there is a pronounced leak from the arterial system during systole Arteriograms in well developed cases show an abrupt upstroke measuring 0 05 to 0 07 second from the onset to the beginning of the blunt peak the peak itself is relatively brief occupying another 0 05 to 0 07 second the

down stroke proper is early beginning about 0 12 second after the onset of the pulse wave and tends to be precipitous (fig 10 01)

The *jugular venous pressure* is not infrequently raised in mitral incompetence when the pulmonary vascular resistance and heart rate are normal and when both pericardial effusion and tricuspid valve disease have been excluded In cases with normal rhythm *a* and *v* are about equal in amplitude and in those with atrial fibrillation the large *v* wave is followed by a steep *y* descent and conspicuous *y* trough In other words the form of the venous pulse is the same as that seen in congestive heart failure Under the circumstances mentioned a similar rise of venous pressure is rarely seen in cases of mitral stenosis Whether myocarditis or myocardial fibrosis is responsible, serious mitral incompetence signifying a more vicious primary rheumatic attack than simple stenosis or whether the phenomenon should be attributed to a filling defect of the right ventricle (Bernheim s syndrome) awaits solution In a typical example necropsy showed a huge dilated left ventricle a normal pulmonary artery a small right ventricle a normal tricuspid valve and a large distended right atrium the cavity of the right ventricle being greatly reduced by the bulged interventricular septum (fig 10 02) In the majority of mixed cases of mitral stenosis and incompetence a high venous pressure is associated with a high pulmonary vascular resistance around 6 to 9 units

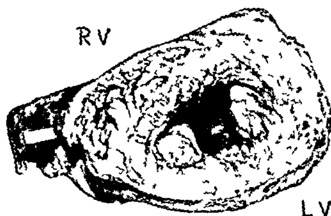
The *cardiac impulse* at the apex beat is hyperdynamic and displaced to the left and can hardly be confused with the impalpable left ventricle of mitral stenosis. If it is suspected that a very large right ventricle might be occupying the apex beat the question can be settled at once by consulting the electrocardiogram

On *auscultation* the characteristic signs of mitral incompetence are absence of a presystolic murmur a soft or normal first heart sound a loud apical pan systolic murmur embracing both first and second heart sounds and often accompanied by a palpable thrill absence of the opening snap of mitral stenosis a loud third heart sound and a short or absent mitral diastolic murmur

A *presystolic murmur* implies appreciable late ventricular filling and is *incompatible* with serious mitral incompetence

A loud *mitral first sound* with a normal P R interval or with atrial fibrillation implies a powerful potential or factual pressure gradient across the valve immediately before the left ventricle contracts a situation that is also incompatible with serious incompetence

The *systolic murmur* of mitral incompetence is usually loud and of fairly high frequency so that it is best heard with the Bowles type of stethoscope it is maximal at the apex beat over the surface of the left ventricle and outwards towards the axilla sometimes it is transmitted posteriorly over the surface of a greatly dilated left atrium The murmur necessarily begins with the mitral component of the first heart sound (fig 10 03) for the leak must commence as the valve tries to close This is some 0 05 second




(a) Transverse section showing great enlargement of the left ventricle and a small right ventricle




(b) Showing great distension of the right atrium

Fig 10 02—Photographs illustrating the Bernheim phenomenon in a fatal case of severe mitral incompetence

the aortic valve opens Again mitral incompetence must continue well into if not beyond the time of aortic valve closure for there is still a strong pressure gradient across the mitral valve at that moment, only as the rapidly falling left ventricular pressure approaches that in the left atrium should the leak stop (Brigden and Leatham 1953) Aortic systolic murmurs heard over the left ventricular apex beat start and finish earlier as described elsewhere (Leatham 1951) Tricuspid systolic murmurs heard over the right ventricular apex beat are also pan systolic but are accentuated during inspiration The pan systolic murmur of ventricular septal defect may be clinically identical with the mitral murmur in quality and timing but ordinarily occurs at the Roger area, well away from the apex beat when the heart is rotated clockwise in cases of ventricular septal defect however or anticlockwise in cases of mitral incompetence confusion is inevitable

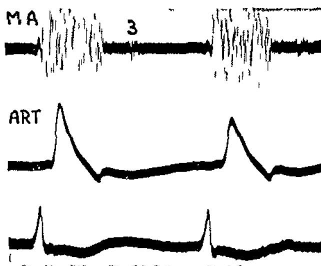



Fig. 10 03—Phonocardiogram in a case of mitral incompetence showing a pan systolic murmur and accentuated third heart sound (top tracing) The murmur starts with the mitral first sound well ahead of the arterial pulse (middle tracing) the electrocardiogram is seen below

The *absence of the opening snap* in serious mitral incompetence is generally attributed to the rigidity of the whole valve mechanism for there is certainly a sufficiently high pressure built up in the left atrium during ventricular systole to snap back the aortic cusp of the mitral valve as the pressure gradient between ventricle and atrium is abruptly reversed in early diastole This fibrous ankylosis also ensures a soft first heart sound even when the P R interval is short or after brief diastolic periods in cases with atrial fibrillation Heavy calcification so common in mixed cases enhances the effect (Wynn 1953)

A *third heart sound* usually loud was heard in 85 per cent of the author s series and is attributed to unusually rapid left ventricular filling Its occurrence in mitral incompetence was noted long ago by Sprague and White (1926)

Not enough attention is paid to the *duration of the mitral diastolic murmur* A murmur that completely fills diastole at a normal heart rate categorically denies serious mitral incompetence for a long murmur means prolonged left ventricular filling Again a short atrio ventricular diastolic murmur is characteristic of unusually rapid ventricular filling whether the relevant atrioventricular valve is diseased or not as in thyrotoxicosis anæmia patent ductus, ventricular septal defect and atrial septal defect In serious mitral incompetence *the short murmur is often loud because the diseased* valve increases the turbulence set up by the torrent of blood that pours through the mitral orifice as soon as it opens but the flow virtually ceases almost as abruptly as it starts long before the next ventricular contraction because the ventricle is rapidly distended and the filling pressure falls off steeply Thus a short mitral diastolic murmur, far from invalidating a diagnosis of pure mitral incompetence, is characteristic of it In cases of heavily calcified mitral valve disease with atrial fibrillation the length of the diastolic murmur and the presence or absence of the third heart sound become the only two auscultatory signs of any diagnostic significance for the pan systolic murmur gives no quantitative information and the absent presystolic murmur soft first heart sound and absent opening snap merely confirm the two circumstances mentioned

*The electrocardiogram*

In well developed cases the electrocardiogram shows an unobtrusive P mitrale and left ventricular preponderance (fig 10 04) In mixed border line cases of stenosis and incompetence with a pulmonary vascular resist ance of 6 to 9 units slight right ventricular preponderance may be seen

## RADIOLOGICAL APPEARANCES

The chief characteristics of mitral incompetence are an enlarged hyper *dynamic, rapidly filled left ventricle associated with considerable dilatation* and conspicuous pulsation of the left atrium (fig 10 05) In the anterior view the left atrium may be seen expanding during ventricular systole both *to the left and right (fig 4 42) It has become fashionable to deride this* sign but I have never seen the left atrium behave in this way in mitral stenosis or in any other condition In the first oblique view systolic expansion of the left atrium is common in mitral stenosis particularly when there is atrial fibrillation but even then the movement is not so abrupt nor the excursion so great as it often is with free incompetence Aneurysmal dilatation of the left atrium is also in favour of incompetence — although it may occur occasionally with pure stenosis The larger the left

Fig 10 04—The electrocardiogram in a case of severe mitral incompetence showing considerable left ventricular preponderance



Fig 10 05—Radiological appearances in a case of severe mitral incompetence showing considerable dilatation of the left atrium and left ventricle and marked pulmonary venous congestion

atrium, the less does it pulsate because the amount of regurgitant blood represents a smaller percentage of the left atrial volume

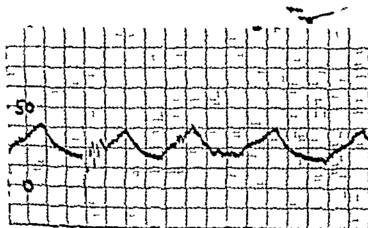
The aorta is usually rather small but less so than in mitral stenosis The pulmonary artery is rarely dilated except in cases of combined stenosis and incompetence with moderate elevation of the pulmonary vascular resistance The right atrium may be dilated if the venous pressure is raised as described previously Pulmonary venous congestion may be marked in severe cases especially when there is left ventricular failure but in the average case it is inconspicuous Heavy calcification of the mitral valve occurs in 50 per cent of cases with combined stenosis and incompetence but is uncommon with pure incompetence

Many attempts have been made to record the movements of the left atrium graphically either by means of electrokymography (e g Luisada and Fleischner 1948) or indirectly by means of an œsophageal pressure pulse tracing (e g Lassar and Loewe 1952 Zoob 1954) On the whole such methods have proved disappointing and have been discarded in most clinics perhaps prematurely

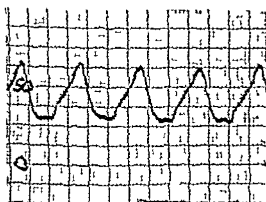
## *PHYSIOLOGICAL FINDINGS*

Cardiac catheterisation usually reveals a raised left atrial pressure a normal or slightly raised pulmonary vascular resistance and a normal or low cardiac output The indirect left atrial pressure tracing obtained by the wedged catheter technique rewards careful study For several years these tracings did not seem to distinguish mitral stenosis from incompetence but attention had always been directed to the systolic part of the curve After studying the y descent of the venous and right atrial pressure pulses in a variety of conditions including tricuspid incompetence and tricuspid stenosis it was gradually established that the higher the filling pressure the steeper was the y descent and the more conspicuous the y trough *provided there was no obstruction at the tricuspid orifice* In tricuspid stenosis however the obstruction delayed ventricular filling and prevented rapid equalisation of atrial and ventricular pressures so that the y descent was relatively slow and the y trough inconspicuous indeed with severe stenosis there was no y trough at all the right atrial pressure continuing to fall after the v peak until interrupted by the next atrial or ventricular contraction a pressure gradient being demonstrable across the tricuspid valve throughout the whole of diastole It seemed virtually certain that obstruction of the mitral orifice would affect the left atrial pressure pulse in the same way i e in mitral stenosis the y descent should be slow and the y trough absent (fig 10 06) whereas in mitral incompetence or left ventricular failure the y descent should be rapid and the y trough conspicuous and early (fig 10 07) Careful analysis of technically satisfactory wedged pressure tracings and direct left atrial pressure tracings obtained at operation confirmed the thesis that obstruction to forward flow retarded

the rate of y descent and since the latter (Ry) was directly proportional to the height of y in all circumstances the degree of obstruction to forward flow was expressed as a ratio Ry/y, Ry being measured in mm. Hg per second and y in mm Hg above the sternal angle In mitral stenosis the




Before valvotomy Ry/y = 1.3




After valvotomy Ry/y = 3.3

Fig. 10.6—Left atrial pressure pulse before and after mitral valvotomy showing a change in the Ry/y ratio from 1.3 to 3.3 after relief of the obstruction

ratio was commonly between 0.6 and 1.0 the extreme upper limit compatible with obstruction to forward flow being 1.6 (Owen and Wood 1955) In pure mitral incompetence left ventricular failure and Pick's disease the ratio usually lay between 2 and 6 Difficult borderline cases had ratios close to 1.6 It should be clearly understood that the Ry/y ratio is an index

of obstruction to forward flow only and that a figure demonstrating the absence of such obstruction does not distinguish mitral incompetence from left ventricular failure It has already proved its value, however, in helping to distinguish between dominant stenosis and dominant incompetence when both are present

*Selective angiocardiography* through a needle inserted directly into the left atrium through the posterior chest wall in the eighth intercostal space close to the vertebral column may show mitral incompetence clearly and gives a good idea of the actual size of the mitral aperture in systole and diastole (Bjork *et al* 1955)

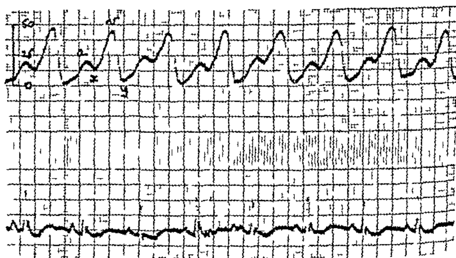


Fig 10 07—Left atrial pressure pulse in a case of mitral incompetence showing a very rapid y descent and conspicuous v trough the Ry v ratio is [illegible]

## *COMPLICATIONS*

Pulmonary œdema hæmoptysis, angina pectoris and systemic embolism have already been discussed under *symptoms*

*Atrial fibrillation* is found in about a third of any average series of cases and is closely related to the age of the patient The great majority of patients over 50 years of age fibrillate Cases of mixed stenosis and incompetence fibrillate more than twice as frequently as cases of pure incompetence and more than one and a half times as frequently as cases of pure stenosis This may be a consequence of the greater severity of the original rheumatic onslaught in the mixed group or because the left atrium tends to be larger in these cases

The ventricular rate may be difficult to control with digitalis in severe cases of mitral incompetence with atrial fibrillation possibly because of the hyperdynamic behaviour of the left ventricle It may be worth pointing out that this difficulty is common to all hyperkinetic circulatory states complicated by atrial fibrillation, whether the left right or both ventricles

are involved, thus it may be encountered in patent ductus atrial septal defect and thyrotoxicosis to give an example from each group

*Bacterial endocarditis* seems to have a predilection for cases of mild mitral incompetence and may offer tragic proof of the organic nature of an apical systolic murmur hitherto regarded as functional Though the infection may be cured by means of penicillin or other antibiotics much damage has usually been inflicted by the time it is brought under control and serious mitral incompetence usually results

### *TREATMENT*

No operative treatment yet devised has been of the slightest benefit to cases of mitral incompetence although heroic efforts have been made to repair the leak (e g Logan and Turner 1952) Nevertheless mitral incompetence is a simple mechanical fault and must remain a constant challenge to surgeons until it can be properly dealt with

Medical treatment and management are essentially the same as for mitral stenosis (q v )

## MITRAL STENOSIS

### *INCIDENCE*

Mitral stenosis with or without an unimportant leak is four times as common as virtually pure mitral incompetence and twice as common as combined stenosis and incompetence it accounts for 64 per cent of all cases of chronic mitral valve disease and for about 54 per cent of all cases of chronic rheumatic heart disease There are at least 100 000 cases of mitral stenosis in Great Britain between the ages of 18 and 44 and four fifths of them will require surgical treatment sooner or later (Wood 1954)

### *AGE AND SEX*

Cowan and Ritchie (1935) who analysed 2 155 cases found that the frequency of chronic mitral valve disease in each decade up to the fifth was 2 19 21 19 and 16 per cent respectively, a further 23 per cent of cases occurring over the age of 50 The figures seem to be much the same for both stenosis and incompetence and in my own series the average age of all cases in each group was 37

The M F sex ratio for cases with pure mitral stenosis is 4 1 when there is trivial incompetence as well it falls to 3 1 and when there is serious incompetence to 1 1 In pure mitral incompetence males predominate the M F sex ratio then being 3 2 (Wood 1954)

### *LIFE HISTORY*

A previous history of rheumatic fever subacute rheumatism or chorea is obtained in about 60 per cent of cases On the whole the more florid recurrent the original rheumatic state the worse the permanent valve

damage and the more probable serious mitral incompetence Mild cases of pure mitral stenosis for example are twice as likely to have had isolated chorea as recurrent rheumatic fever whereas cases of combined stenosis and incompetence most of which have grossly disorganised valves are ten times more likely to have had recurrent rheumatic fever than isolated chorea

In my own series the average age of the initial rheumatic attack was 12 years the latent symptom free period 19 years the average age of onset of symptoms 31 years and the time spent in each of the first three grades of effort intolerance 2 7 2 7 and 1 94 years respectively total incapacity being reached 7 3 years after the onset of symptoms The average duration of total incapacity was about three years in 644 fatal cases of chronic rheumatic heart disease analysed by de Graff and Lingg (1935) and was *the same for mitral stenosis as for other valve lesions There is of course* considerable variation in individual cases but the general trend cannot be ignored

## *PATHOLOGY*

Brock (1952) has referred to the monotonous regularity with which most cases of mitral stenosis submitted to operation have a small oval orifice measuring $1 \times 0\ 5$ cm In the simplest cases of pure stenosis the chief points of fusion are where the shortest stoutest and most direct chordæ tendineæ arising from the very summit of the papillary muscles join the margins of the cusps on each side of what Brock has called the central pathway of the mitral valve These two critical areas of tendon *insertion are about 2 cm apart which means that the central pathway* through which most of the blood normally enters the left ventricle is only about 3 sq cm in cross section and lateral to this there is relatively little flow the commissures acting merely as hinges allowing the central parts of the cusps to open widely In a mild attack of rheumatic carditis the only damage to the valve may be along the line of closure of the cusps just proximal to their free margins where they receive the maximum natural trauma Perhaps as the result of deposition of platelets and fibrin on the surface of this damaged zone a stickiness develops which encourages the two cusps to adhere to one another where they meet most firmly The strong blood flow through the central pathway prevents fusion at the centre but there is less resistance to fusion at the critical areas of tendon insertion on each side of the central pathway and there is good reason to believe that this is where the two cusps first stick together The lateral parts of the valve are usually spared in a mild attack of rheumatic fever and have no reason to adhere of themselves nor has lateral fusion alone ever been observed Once the two cusps are held together at the critical *areas of tendon insertion* however *their lateral parts necessarily come into* permanent apposition and since there is little or no flow in this zone to prevent it light lateral adhesions then form The result is fusion of the

two cusps from the ring to the edges of the central pathway Since the hinge like action of the lateral parts of the valve can no longer function the central portion of the two cusps cannot open fully the aperture thus becomes oval and cannot measure much more than 2×1 cm in the mildest cases Gradual reduction in the size of the lumen between the two critical areas of tendon insertion may result from repeated deposits of fibrin at the edges the excrescences becoming covered by endothelium and then fibrosed as described by Magarey (1951)

This attractive hypothesis so ably presented by Brock (1952) leaves one important question and its corollaries unanswered When does cross fusion of the critical areas of tendon insertion occur? If it is during the stage of active carditis which the hypothesis favours why does the initial 2×1 cm stenosis give rise to no physical signs? There is ample proof that a presystolic murmur and loud first heart sound occur when stenosis is trivial the cardiac output normal and the left atrial pressure around 5 mm Hg with reference to the sternal angle If on the other hand the stenosis develops when it seems to i e some 5 to 10 years after the initial attack why should sudden fusion of the critical areas of tendon insertion occur then at a time when the surface of the cusps should have no cause for stickiness? If the hypothesis is correct it would seem that initial fusion of the critical zones would have to occur during the active stage but that this would not result in physiological stenosis This is quite likely especially if the initial points of fusion were 2 5 cm apart for the central pathway of the mitral valve would then be as large as the aortic orifice assuming that the central parts of the cusps were able to open widely enough Physiological stenosis with a pressure gradient across the valve would then develop slowly and variably over the years according to the speed with which the commissures of the oval orifice gradually silted up From experience gained at operation mild physiological stenosis, with typical physical signs but no symptoms occurs when the oval orifice is between 1 5 and 2 cm in length and perhaps half this in width Critical stenosis requiring valvotomy is associated with an oval orifice averaging 1× 0 5 cm, as repeatedly pointed out by Brock By extreme stenosis is meant an orifice materially smaller than this in the region of 5×3 mm Although Brock has criticised the terms mild average and severe stenosis when used with the intention of conveying some idea of the degree of stricture present rather than the patient s disability in the author s view their use with just this meaning is thoroughly justified A simple mathematical sum will show that a relatively mild stenosis measuring 1 5×0 75 cm is more than twice as large as an average orifice of 1×0 5 cm and nearly eight times as large as a severe stricture measuring 5×3 mm

Whether gradually increasing stenosis results chiefly from the effects of continued smouldering activity or whether it is a more or less inevitable secondary change due to repeated deposition of fibrin on a damaged area has yet to be settled

*HÆMODYNAMICS*

Initial cross fusion of the critical areas of tendon insertion during the stage of active carditis leaves a sufficiently large central pathway probably measuring 2 5×1 5 cm through which a normal blood flow can be maintained without any form of compensation According to the Gorlin formula—such an orifice which would measure about 2 5 sq cm in cross section would allow a blood flow of 6 8 litres per minute with a left ventricular filling pressure of 6 mm Hg and a heart rate of 70 to 80 beats per minute As the commissures of this oval orifice gradually silt up the size of the aperture dwindles until it begins to obstruct the blood flow The left atrial pressure then rises a few mm Hg and wholly compensates for the obstruction It is calculated that an oval orifice measuring 2–2 25×1 cm is small enough to cause this grade 1 physiological stenosis Physical signs (presystolic murmur and accentuated first heart sound) first develop at this stage which is ordinarily some 3 to 10 years after the original rheumatic attack Grade 2 or moderate stenosis implies an oval aperture measuring 1 5–1 75×0 75–0 9 cm This too is easily compensated for by a further rise of left atrial pressure which at rest is found to be around 10 mm Hg above the sternal angle Under ordinary circumstances there are no symptoms but *the auscultatory physical signs of mitral stenosis are now complete*, the opening snap being easily heard and the mitral diastolic murmur occupying practically the whole of diastole The elevated left atrial pressure is associated with a similar rise of pulmonary venous pressure pulmonary capillary pressure and pulmonary arterial pressure the pulmonary arterio venous pressure gradient remaining normal (about 10 mm Hg)

On strenuous exercise there is some danger of unexpected acute pulmonary œdema in these cases of moderate severity for no protective mechanisms have yet come into play It may be calculated for example that a cardiac output of 16 litres per minute with a heart rate of 120 would raise the left atrial pressure to 35 mm Hg above the sternal angle if the mitral aperture was 1 5 cm With no acquired barrier between pulmonary capillaries and alveoli a capillary pressure of this level *which is above the* osmotic pressure of the plasma must cause pulmonary œdema Practical *experience supports these statements*

Grade 3 or considerable stenosis is the classic text book type According to Brock and other surgeons the valve in these typical dyspnœic cases measures about 1×0 5 cm but physiological calculations suggest it is more likely to have a cross section of 0 75 sq cm which means dimensions nearer 1 5×0 75 cm Dexter s group puts the critical orifice at 1 cm² which implies an oval aperture measuring about 1 75×0 85 cm (Lewis *et al* 1952) [The discrepancy between physiological calculations and surgeons estimates is consistent with all grades of stenosis Post mortem measurements are closer to physiological expectations ] *Under these circumstances* an adequate cardiac output can only be maintained with a

left atrial pressure around 20 to 25 mm Hg above the sternal angle at rest This causes pulmonary venous congestion and its consequences Exercise excitement pregnancy or simple tachycardia (which diminishes the ventricular diastolic filling time) results in considerable further elevation of the pulmonary venous pressure which may rise well above the osmotic pressure of the plasma (30 mm Hg) At this stage a proportion of patients die from acute pulmonary œdema but the majority do not because certain mechanisms come into play which serve to protect the lungs and it is important to understand just what these are

If the mean left atrial pressure is 30 mm Hg the mean pressure in the pulmonary artery must be at least 40 mm Hg if the necessary gradient between the two is to be preserved In acute experiments this passive pulmonary hypertension as it may be called maintains a linear relationship to the left atrial pressure at all levels (Lasser and Loewe 1954) and this is the rule in chronic cases (Wood 1954) In 28 per cent of individual however as soon as the left atrial pressure begins to rise at all seriously the pulmonary arterioles constrict This obstructs the circulation proximal to the pulmonary capillaries and so prevents their developing dangerously high pressures In response to the high pulmonary vascular resistance the pulmonary blood pressure rises considerably and may reach systemic level This puts a heavy burden on the right ventricle which sooner or later fails Thus by this mechanism early death from acute pulmonary œdema is prevented at the cost of a low cardiac output and ultimate right ventricular failure

A second change that tends to prevent pulmonary œdema is the development of a physical barrier between the capillaries and alveoli the capillary wall interstitial tissue and alveolar basement membrane all becoming thickened so that it becomes increasingly difficult for fluid to enter the alveoli even though it may pass into the interstitial tissue (Hayward 1955) This helps to explain why acute pulmonary œdema is usually an early symptom and why attacks tend to cease spontaneously if life can be preserved long enough for this barrier to be erected Fluid is removed from the interstitial tissue by the lymphatics which themselves become engorged

The very high left atrial pressures that may develop on exercise in these stereotyped cases of mitral stenosis even as high as 60 mm Hg seem to *deny the importance of a broncho pulmonary venous shunt mechanism* which theoretically might relieve pulmonary venous congestion According to Marchand Gilroy and Wilson (1950) the true bronchial veins within *the substance of the lung drain directly* into the pulmonary veins so that the bronchial venous pressure must be the same as the pulmonary venous pressure This may explain early hæmoptysis in mitral stenosis but provides no basis for belief in a shunt mechanism that might relieve the pulmonary venous pressure However these workers also confirmed that the extrapulmonary bronchial veins which they called the pleuro hilar veins drained into the azygos hemiazygos and intercostal veins and

communicated freely with the pulmonary veins as previously described by Miller (1947) and others in mitral stenosis the pleuro-hilar bronchial veins were dilated and sometimes tortuous and varicose (Gilroy Marchand and Wilson 1952) It must be admitted then that the pulmonary venous circulation is in fact provided with a safety valve at the root of the lung and that when well developed this could lower the pulmonary venous pressure at the expense of the cardiac output Patients relieved of pulmonary congestion in this way should complain of fatigue and perhaps œdema when the pulmonary venous pressure is only moderately raised the pulmonary vascular resistance normal and the estimated cardiac output normal when based on an A V difference calculated from samples obtained from the pulmonary artery right ventricle or right atrium From such physiological data the physician would conclude that stenosis was mild and that the symptoms must have some other explanation Only unexplained enlargement of the right ventricle might point to the true state of affairs unless samples obtained from the superior vena cava above and below the junction of the azygos vein proved the existence of a significant broncho pulmonary shunt as when an anomalous pulmonary vein joins the azygos No physiological studies on this point have yet been reported but two observations may be mentioned (1) I have not myself been able to detect much difference between high and low superior vena cava samples in several cases of mitral stenosis in which the possibility of a broncho pulmonary shunt was considered (2) in the few cases of mitral stenosis in which unexplained enlargement of the right ventricle has been associated with a relatively low pulmonary venous pressure and a normal pulmonary vascular resistance the cardiac output based on routine pulmonary artery samples has been low and has failed to rise properly on exercise so that a myocardial fault has been invoked (Harvey *et al* 1955) This myocardial dysfunction may be due to active carditis or residual fibrosis, and may be regarded as the fourth factor that tends to protect the lungs

To sum up it must be repeated that in the typical case of critical mitral stenosis the usual problem is not why the pulmonary venous pressure is lower than expected but why pulmonary œdema does not develop when the pulmonary venous pressure rises well above the osmotic pressure of the plasma and the answer to this may lie in the development of a physical barrier between the capillaries and alveoli A high pulmonary vascular resistance explains the behaviour of the vast majority of cases in which elevation of the left atrial pressure is limited the right ventricle large and the cardiac output low and a myocardial fault adequately explains the remainder There may or may not be a small group of cases that are materially influenced by the development of a broncho pulmonary venous shunt This might be best detected by analysing low S V C samples for traces of Evans blue dye a few seconds after injecting a suitable quantity into the pulmonary artery

## SYMPTOMS

The chief symptom of mitral stenosis is *dyspnœa* This appears to be due to increased rigidity of the lungs so that the intrathoracic pressure swings have to be greater than normal in order to inflate and deflate the lungs (Marshall McIlroy and Christie 1954) in other words respiration becomes laborious and ventilation on effort readily approaches 50 per cent of the maximum breathing capacity The increased rigidity is apparently caused by changes in the interstitial tissue including chronic interstitial œdema (Hayward 1955) for the pulmonary blood volume is normal (Lagerlof *et al* 1949) The extra space occupied by the interstitial tissue reduces the vital capacity and total lung volume Œdema of the bronchial mucosa with or without broncho spasm due to the high intrapulmonary bronchial venous pressure (Marchand *et al* 1950) adds to the ventilatory difficulty Except during attacks of acute pulmonary œdema the arterial pO pCO and pH are usually normal Whether stretch receptors are stimulated by the changes in the interstitial tissue and excite the Hering Breuer reflex inhibiting the depth of inspiration is uncertain

The degree of dyspnœa on effort usually determines the clinical grading of effort intolerance in mitral stenosis Four grades are commonly recognised corresponding to the four adjectives of degree—slight moderate considerable and gross In grade I symptoms are provoked by more than average activity e g running hurrying walking up hills playing games polishing or scrubbing Patients in this grade usually undertake the activities that make them breathless but cannot compete with their fellows In grade II symptoms occur on ordinary activity such as walking at an average pace or up two flights of stairs carrying a shopping basket dancing and any form of manual labour Patients in this grade limit their physical activities but can still lead an almost normal social life In grade III symptoms develop with less than ordinary physical activity and force patients to walk slowly on the level shopping and all but the lightest housework is abandoned Grade IV means total incapacity

*Orthopnœa* occurs in 70 per cent of cases in grades III or IV Sitting up especially with the legs down lowers the right atrial pressure and thus diminishes the output of the right ventricle This in turn lowers the left atrial pressure and therefore the pulmonary venous and capillary pressures In the horizontal position these effects are reversed so that transudation of fluid from the pulmonary capillaries into the interstitial tissue is encouraged Although Donald *et al* (1953) have denied that sitting up in bed lowers the cardiac output sufficiently to be of any importance they noted that in cases of mitral stenosis it resulted in a marked fall of pulmonary artery pressure which certainly suggests a drop in output

*Attacks of frank pulmonary œdema* occur in about 10 per cent of all cases of mitral stenosis in which the mitral orifice is more or less critically reduced (Wood 1954) Precipitating agents include effort emotion sexual intercourse pregnancy respiratory infections uncontrolled atrial fibrilla

tion and anæsthesia Physiologically the most important provocative factors are tachycardia, which reduces the left ventricular diastolic filling time hydræmia a rise of cardiac output and perhaps some neurogenic or chemical disturbance which alters capillary permeability Physiological data during an attack are necessarily limited but the left atrial pressure is usually between 30 and 50 mm Hg and always well above the osmotic pressure of the plasma the heart rate is nearly always 120 or more beats per minute the cardiac output is higher than usual and the pulmonary vascular resistance commonly normal The transudate is believed to be much the same kind of fluid that normally passes through the capillary walls into the tissue spaces which in the interstitial tissues of mammalian lung contains 2 5 to 3 G per cent of protein (Warren and Drinker, 1942 Drinker 1945) As the attack proceeds the arterial oxygen saturation gradually falls and in severe cases may become as low as 50 per cent at the beginning of the attack, however it is normal so that anoxia cannot be blamed for initiating events by increasing the permeability of the capillary walls By having this effect later in the attack, however anoxia could well establish a vicious circle were it not for the fact that it also causes a sharp rise of pulmonary vascular resistance (Liljestrand 1948) which must tend to lower the capillary pressure and terminate the attack Limited evidence that the pulmonary vascular resistance does not rise during spontaneous attacks of pulmonary œdema should be accepted with considerable reserve because these cases are very difficult to investigate

Protective mechanisms or complications tending to prevent acute pulmonary œdema include a high pulmonary vascular resistance the development of a capillary alveolar interstitial barrier atrial fibrillation when controlled by means of digitalis, myocarditis or cardiac fibrosis, associated tricuspid stenosis and perhaps a broncho pulmonary venous shunt

The most important of these is probably a high pulmonary vascular resistance In my own series this averaged 2 9 units in cases giving a history of pulmonary œdema and never exceeded 5 2 units whereas in patients who had never had orthopnœa paroxysmal dyspnœa or frank pulmonary œdema but whose stenosis was no less severe it averaged 9 2 units

Clinically acute pulmonary œdema occurs characteristically in young women with an average grade of stenosis relatively early in its course before protective mechanisms have had time to develop Thus the average age of patients with pulmonary œdema in the author s series was 32 compared with 37 for the series as a whole Normal rhythm is nearly twice as frequent as atrial fibrillation despite the fact that the onset of the latter may precipitate acute pulmonary œdema The attack itself may start insidiously with slight dyspnœa orthopnœa and a gentle repetitive cough (stage A) but soon develops strongly dyspnœa becoming extreme and often accompanied by wheezing (cardiac asthma) the face pales the heart rate quickens the blood pressure rises, the extremities turn cold and blue and the heart

pounds (stage 2) The patient becomes greatly distressed and frightened and as suffocation increases fine crepitations become widespread and quantities of frothy white or pink fluid may be expectorated (stage 3) Central cyanosis appears late in the attack, and if the arterial oxygen saturation falls sufficiently the vasomotor centre may fail, and a state of collapse sets in the blood pressure falls the skin becomes grey cold and wet the pulse almost imperceptible and the respirations shallow (stage 4) If treatment fails the patient finally sinks into a state of unconsciousness and dies

Paroxysmal cardiac dyspnœa is similar, but transudation of fluid from the capillaries does not enter the alveoli being prevented from doing so by the physical barrier described earlier Interstitial œdema makes the lungs very rigid and breathing is laboured but there are no crepitations no fluid is expectorated and the arterial oxygen saturation falls little if at all

Thus orthopnœa paroxysmal cardiac dyspnœa and acute pulmonary œdema are all manifestations of a tendency for fluid to pass out of the pulmonary capillaries into the interstitial tissue of the lung Although from the patient s point of view the order in which they have just been given represents an increasing grade of severity, the disease as a whole is usually most advanced when there is orthopnœa only, and least advanced when there are attacks of acute pulmonary œdema cases of paroxysmal cardiac dyspnœa occupying a middle position The reason for this has already been explained

*Hæmoptysis*

There are five kinds of hæmoptysis complicating mitral valve disease (1) the sudden unexpected profuse hæmorrhage known as pulmonary apoplexy (2) blood streaked mucoid sputum associated with winter bronchitis (3) blood stained sputum associated with attacks of paroxysmal cardiac dyspnœa (4) pink frothy sputum accompanying acute pulmonary œdema (5) frank hæmoptysis due to pulmonary infarction

A history of *pulmonary apoplexy* is obtained in one quarter of cases severe enough to warrant valvotomy It is characteristically an early symptom often the very first and although usually recurrent attacks tend to cease spontaneously after two or three years The most important precipitating agents are pregnancy and physical effort but at least half of the attacks occur without warning and for no reason known to the patient

The hæmorrhage itself is sudden and profuse the amount of blood coughed up being usually measured in ounces It is rarely dangerous and tends to stop spontaneously within half an hour or so although residual blood may stain the sputum for a day or two

Pulmonary apoplexy is attributed to rupture of a small intrapulmonary bronchial vein as a result of a rather sudden rise of left atrial pressure for which the pulmonary and bronchial venous systems are unprepared In the early stage of mitral stenosis as in normal individuals these vessels

are very thin walled after being subjected to an increased pressure for several years however their walls thicken appreciably (Henry 1952) and this may be one reason why attacks occur relatively early and after two or three years tend to cease spontaneously Rupture of a dilated pleuro hilar vein which is in anastomotic communication with the pulmonary venous system is another and perhaps more likely source of profuse hæmorrhage for these small veins are forced to carry more than their fair share of blood and though not subjected to high pressure are often varicose (Gilroy *et al* 1952) The fall in pulmonary venous pressure likely to result from a brisk hæmorrhage may well discourage further bleeding

As pointed out by Thompson and Stewart (1951) hæmoptysis of this kind is not a sign of pulmonary hypertension On the contrary it is exceedingly rare when the pulmonary vascular resistance is over 10 units for the pulmonary venous system is then protected (Wood 1954)

*Congestive hæmoptysis* is a convenient title for blood stained sputum accompanying an attack of acute bronchitis paroxysmal dyspnœa or pulmonary œdema The mild hæmorrhage in these cases is never as important as the condition with which it is associated The ruptured vessels are presumably very small for hæmorrhage is never profuse with bronchitis and paroxysmal dyspnœa a bronchial vessel is almost certainly at fault with acute pulmonary œdema however the uniformly pink froth suggests capillary rupture into alveoli

*Hæmoptysis due to pulmonary infarction* is a late complication of mitral stenosis and is usually caused by an embolus secondary to phlebo thrombosis in the legs in advanced cases with heart failure This will be discussed later

*Winter bronchitis*

Recurrent attacks of winter bronchitis occur in about a third of cases of well developed mitral stenosis Cough with blood stained sputum wheezing and breathlessness may be very distressing The turgid or œdematous state of the bronchial mucosa caused by the high bronchial venous pressure is believed to be responsible for the severity of symptoms if not for the susceptibility to infection although a convincing relationship between the frequency of bronchitis and the height of the left atrial pressure cannot be demonstrated statistically (Wood 1954) Compression of the left bronchus by a greatly dilated left atrium which has been known to cause collapse of the left lung (King 1838) or splaying of either bronchus plays little part in the syndrome

It is unusual for recurrent bronchitis to have any permanent ill effect on lung function or the pulmonary circulation in cases of mitral stenosis and fears that bronchitis may be primary or that secondary bronchitis has already caused emphysema and cor pulmonale are rarely justified On the contrary one of the many remarkable results of technically successful valvotomy is the abolition of these tiresome attacks

### *Systemic embolism*

In any large series of living cases of mitral stenosis a history of systemic embolism is likely to be obtained in 9 to 14 per cent (Sellors Bedford and Somerville 1953 Wood 1954) The embolism is cerebral in at least 60 per cent of instances visceral in 10 per cent and peripheral in 30 per cent In about 20 per cent of afflicted cases emboli are multiple and in 60 per cent recurrent (Daley *et al* 1951 Wood 1954)

Atrial fibrillation is a contributing factor in about three quarters of all cases and is particularly dangerous at its onset when the ventricular rate is uncontrolled

Little correlation has been found between the size of the left atrium or of its appendage and the frequency of embolism and giant left atria are rarely to blame There is no correlation between the incidence of embolism and the pulmonary vascular resistance or the size of the mitral orifice Embolism may be the first symptom of mitral stenosis occurring at a time when there is no effort intolerance and when the rest of the data indicate a relatively mild stricture this was so in 12 5 per cent of embolic cases studied by the author

At operation a clot in the left atrium or its appendage is found in about 22 per cent of all cases whether there has been a history of embolism or not Left atrial thrombi are admittedly nearly twice as common in post mortem material (Wallach *et al* 1953) but even then some 36 per cent of cases with a history of embolism have none (Daley *et al* 1951) Operative embolism the frequency of which has dwindled from 10 to 5 per cent as more effective precautionary measures have been taken is no more common in patients with a history of embolism than in those without

All this suggests that only fresh clots are likely to be flung out into the systemic circulation and that once a thrombus is organised there is no further spontaneous danger from that source only the surgeon s finger is liable to dislodge a fragment of old thrombus

The local effects of systemic embolism have been described briefly in chapter I It may be added here that out of 20 cases of cerebral embolism occurring in patients already under observation in mitral valve disease only two died and that the 49 per cent mortality cited by Daley *et al* (1951) may well be biased by selected and post mortem material When trying to prevent cerebral embolism during valvotomy both carotids should be temporarily occluded at critical moments because experimental and necropsy evidence proves that emboli may pass into either carotid impartially (Hall Dencker and Biorck 1952)

### *Angina pectoris*

Cardiac pain indistinguishable in all respects from that encountered in occlusive-coronary disease occurs in about 10 per cent of cases of mitral stenosis that are otherwise severe enough to warrant valvotomy it does not occur in mild cases The angina is not caused by coincidental coron

atherosclerosis because the sex ratio of affected cases is 5 1 in favour of women, their average age is 36 pain always disappears following technically successful valvotomy and in a limited number that have come to necropsy the coronary arteries have been normal Angina is twice as common in cases with a high pulmonary vascular resistance as in those without and also twice as common in cases with extreme stenosis as in those with an average stricture It is tentatively attributed to functional impairment of the coronary blood flow due to strict limitation of the cardiac output and is believed to affect the left ventricle more than the right as long as the pulmonary artery pressure on effort is lower than the aortic (Wood 1954)

*Left vocal cord paralysis* (Ortner s syndrome)

Huskiness of the voice due to paralysis of the left recurrent laryngeal nerve occurs in about 0 5 per cent of cases of mitral stenosis Ortner (1897) thought that the nerve was compressed by the dilated left atrium and essentially this may be true but the actual compression is usually mediated by enlarged trachea bronchial lymph nodes (Dolowitz and Lewis 1948) and dilatation of the pulmonary artery is often contributory (Fetterolf and Norris 1911) The voice may improve post operatively (Ari Harvey and Hufnagel 1955)

*Atrial fibrillation*

Rapid irregular palpitations in cases of mitral stenosis are commonly due to paroxysmal or uncontrolled atrial fibrillation The abnormality of rhythm occurs in about 40 per cent of all cases and is related chiefly to the age of the patient, not to the degree of stricture (de la Chapelle Graefe and Rottino 1934) My own findings in live cases agreed almost exactly with those of the authors cited in addition left atrial biopsies denied that rheumatic activity played any part in encouraging atrial fibrillation even in the youngest adults and more than average left and right atrial dilatation could be interpreted as a result rather more easily than as a cause of the rhythm change

Uncontrolled atrial fibrillation may cause acute dyspnœa because the rapid heart rate tends to increase the output of the right ventricle while depriving the left of sufficient diastolic time in which to fill it should be understood that shortening diastole interferes little with ventricular filling when the atrioventricular valve is normal but considerably when it is stenosed

When the pulmonary vascular resistance is high atrial fibrillation with a rapid ventricular rate usually causes congestive heart failure the tendency for the left atrial pressure to rise secondary to the increased rate is offset by the diminished right ventricular output so that fatigue œdema and swelling of the abdomen overshadow breathlessness The cardiac output may be very low in these cases because the shortened left ventricular diastolic filling time is not compensated for by an adequate rise of left atrial pressure

When the ventricular rate is controlled by means of digitalis these physiological difficulties are removed and recovery is prompt This is why digitalis has always been especially renowned for the benefit it bestows on cases of *rheumatic heart disease* with atrial fibrillation

The circulatory hold up when the ventricular rate is very fast also explains the frequency of fresh thrombosis in the left atrium at this time and the immediate danger of embolism

## PHYSICAL SIGNS

### *Mitral facies and cold blue hands*

Peripheral cyanosis in the face and hands is due to peripheral vaso constriction secondary to a low cardiac output and is therefore seen especially in cases with a high pulmonary vascular resistance it is not a feature of uncomplicated mitral stenosis of average severity in which a fair output is maintained with the help of a high left atrial pressure In advanced pulmonary hypertensive cases the hands may be warm and the palms bright red as a result of impaired hepatic function

Loss of weight is usual in severe mitral stenosis unless counterbalanced by œdema and the lean features contribute to the mitral facies

### *Peripheral pulse*

The brachial pulse in all well developed cases of mitral stenosis is small in volume but well sustained in quality except in advanced cases with pulmonary hypertension and chronic heart failure when vasodilatation due to impaired hepatic function may modify it

### *Jugular venous pressure and pulse*

In simple mitral stenosis the systemic venous pressure and the jugular pulse are both normal The venous pressure may rise however as a result of improperly controlled atrial fibrillation severe pulmonary hypertension or associated tricuspid stenosis Heart failure due to myocarditis or cardiac fibrosis is rare

With uncontrolled atrial fibrillation the *x* descent of the jugular pulse disappears *v* begins earlier and is followed by *y* so that there is only one crest and one trough per cardiac cycle the higher the *v* wave the quicker the *y* descent and the more conspicuous the *y* trough

Both pulmonary hypertension and tricuspid stenosis usually give rise to a giant *a* wave when there is normal rhythm with atrial fibrillation however cases of pulmonary hypertension show a rapid *y* descent and deep *y* trough whereas cases of tricuspid stenosis show a relatively slow *y* descent and absent *y* trough

### *Cardiac impulse*

The left ventricle is characteristically impalpable in cases of pure mitral stenosis only the tap of the first heart sound being appreciated in the

region of the mid clavicular or anterior axillary line The degree of right ventricular thrust in the left parasternal line is proportional to the pulmonary vascular resistance passive pulmonary hypertension causes very little right ventricular enlargement and a dilated left atrium posteriorly only pushes the heart forwards appreciably when it is aneurysmal Pulsation over the pulmonary artery is rare and when present means an extreme pulmonary vascular resistance

*Auscultation*

There are four important auscultatory signs of mitral stenosis—a presystolic murmur a loud first heart sound an opening snap and a mitral diastolic murmur (fig 10 08)

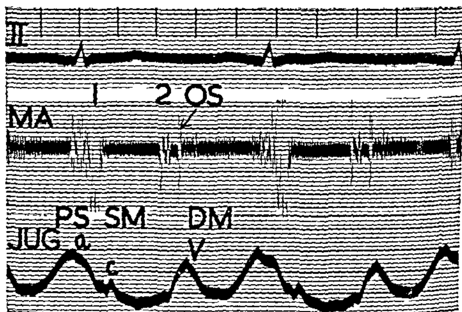



Fig 10 08– Phonocardiogram from a case of mitral stenosis showing a crescendo presystolic murmur loud first sound opening snap and mid diastolic murmur timed against the electrocardiogram and phlebogram

*(By courtesy of Dr ... Aubrey Leatham*

A *mitral presystolic* (Fauvel 1843) *or left atrio systolic* (Gairdner 1861) *murmur* can be heard in practically all cases of physiological mitral stenosis with normal rhythm even when the stricture is so mild as to be associated with a left atrial pressure of only 5 mm Hg above the sternal angle It is occasionally masked by gross enlargement of the right ventricle secondary to an extreme pulmonary vascular resistance for the left ventricle may then be displaced so far posteriorly that mitral events cannot be heard at the apex beat which is usurped by the right ventricle

The *first heart sound is accentuated* in practically all cases of more or less

pure mitral stenosis provided the valve is not heavily calcified In conjunction with the presystolic murmur a loud first sound can be heard in the mildest cases with left atrial pressures only a few mm Hg above the sternal angle The late diastolic or presystolic atrio ventricular pressure gradient forces the mitral cusps to remain wide open to the very end of diastole so that when the left ventricle contracts they slam together Heavily calcified valves are usually so rigid that very little movement of the cusps is possible

In cases with atrial fibrillation the presystolic atrio ventricular pressure gradient and therefore the intensity of the first sound varies inversely with the length of the preceding diastole as pointed out by Ravin and Bershof (1951) Exceptionally however the intensity of the first heart sound does

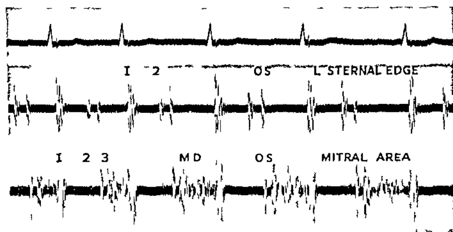



Fig 10 09—Phonocardiogram showing an opening snap followed by a mitral diastolic murmur in a case of mitral stenosis with atrial fibrillation

B ... (D A b ... Le tham)

not vary or it may have a paradoxical relationship to the length of the preceding cycle Such behaviour has not been satisfactorily explained but it suggests relative fixation of the cusps so that they may not be able to billow into the ventricle beyond certain narrow limits whatever the atrio ventricular pressure gradient the intensity of the first sound then varies inversely with the pressure gradient for the cusps close more sharply when the left ventricle is full and the left atrial pressure relatively low than when the left ventricle is half empty and the left atrial pressure high

The first heart sound is also slightly delayed in mitral stenosis because the first 0 01 second or so of systole is occupied with raising the left ventricular pressure to atrial level (Cossio and Berconsky 1943) In cases with atrial fibrillation the delay varies inversely with the length of the preceding cycle (Messer *et al* 1951)

The *opening snap* of Potain is a sharp high pitched sound made by the aortic cusp of the mitral valve when it is flung forwards into the cavity of the left ventricle as the atrio ventricular pressure gradient is reversed at the end of the period of isometric relaxation and therefore coincides temporally with the summit of the *v* wave of the left atrial pressure pulse (Margolies and Wolferth 1932) It occurs 0 06 to 0 14 second (usually 0 08 to 0 10 second) after aortic valve closure (Braun Menendez and Orias 1935) and is best heard down the left sternal border over the root of the aorta or at the apex beat (fig 10 09) The interval between the aortic second sound and the opening snap is inversely proportional to the height of the left atrial pressure and therefore directly proportional to the length of the preceding cardiac cycle (Messer *et al* 1951) Thus if due allowance is made for cycle length (disregarding the cardiac output and the pulmonary vascular resistance), the more delayed the first heart sound and the earlier the opening snap the tighter is the mitral stenosis (Wells 1954)

The opening snap is heard in practically all cases of pure mitral stenosis of more than trivial degree, provided the valve is not heavily calcified and rigid Exceptionally an extreme pulmonary vascular resistance masks the snap because a greatly enlarged right ventricle tends to prevent transmission of mitral sounds to the anterior chest wall The opening snap may also be absent when there is associated aortic incompetence probably because the regurgitant jet interferes with the forward movement of the aortic cusp of the mitral valve

An *apical mid diastolic murmur* is heard in all well developed cases of mitral stenosis unless masked by a greatly enlarged right ventricle or a loud aortic diastolic murmur transmitted to the apex It is usually low pitched and is heard best with the bell stethoscope when the patient lies on the left side The murmur is not prevented by heavy calcification nor altered by atrial fibrillation It begins just after the opening snap its onset coinciding with the period of rapid ventricular filling i e with the steep part of the *y* descent (downstroke of *v*) It therefore gives rise to a form of triple rhythm the cadence of which is very characteristic whether preceded by an opening snap or not

Neither the intensity of the murmur nor the presence of a thrill matters much but *the length of the murmur is very important* In mild cases the murmur is relatively short ending as soon as left atrial and ventricular diastolic pressures equalise in more severe cases it extends right up to the next first heart sound for left atrial and ventricular diastolic pressures do not equalise at all The length of the murmur is easiest to gauge in cases with atrial fibrillation for there is then no interference from atrial systole and from time to time long pauses facilitate analysis

## THE ELECTROCARDIOGRAM

A well defined P mitrale (fig 10 10) is seen in practically all cases of moderate or severe mitral stenosis with normal rhythm but is usually

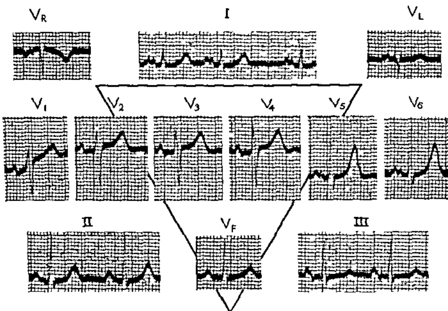



Fig 10 10—Electrocardiogram in a case of mitral stenosi showing \ idened bifid P waves particularly in leads 1 2 $V_5$ and V

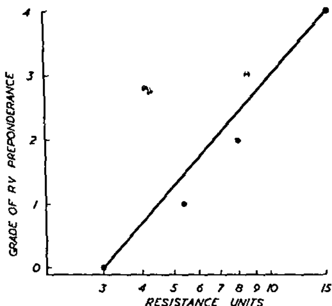



Fig 10 11—Graph show ng th relationship between the electrocardiographic grade of right ventricular prepondera ice and the pulmonary vascular resistance in cases of mitral stenos s (semi logarithmic scale)

absent in mild cases The P wave is bifid and widened to 0 12 second the first peak representing right atrial activation the second left atrial activation (Reynolds 1953) The voltage is usually normal

Tall peaked P waves in cases of mitral stenosis indicate a high pulmonary vascular resistance or associated tricuspid stenosis

The ventricular complexes are strictly normal in uncomplicated cases unless the S T segments are depressed by digitalis therapy Right ventricular preponderance means pulmonary hypertension secondary to a raised pulmonary vascular resistance the degree of each correlating very closely with one another (fig 10 11) Passive pulmonary hypertension does not cause right ventricular preponderance

## *RADIOLOGICAL APPEARANCES*

X rays reveal characteristic changes in the size shape and behaviour of the heart and great vessels and in the appearances of the lungs, which taken together are seen in no other condition

The *aorta* is small unless the patient is over 45 years old or unless the stenosis is sufficiently mild to allow a normal resting cardiac output

The *left ventricle* is inconspicuous hypodynamic and fills relatively slowly Apparent enlargement in otherwise uncomplicated cases of pure stenosis is usually an erroneous interpretation of a shadow that may represent pericardial effusion or a greatly enlarged right ventricle that is occupying the apex beat occasionally it is genuine and may then be due to previous mitral incompetence or unusually severe carditis

*The left atrium is dilated* in all but the mildest cases In the anterior view it may be seen on both borders of the heart forming a hump between the pulmonary arc and left ventricle on the left side and lying above and overlapping the right atrium on the right side (fig 10 12) In the lateral or oblique positions a dilated left atrium displaces the barium filled œsophagus backwards (fig 10 13) Rarely the whole chamber is sharply outlined as a result of endocardial calcification

The degree of left atrial enlargement is not related to the severity of the stenosis The left atrium is apt to be relatively small in cases of pure stenosis *in young adults with normal rhythm and a tendency to develop pulmonary* œdema and in cases with an extreme pulmonary vascular resistance it is larger when there is atrial fibrillation, and especially when there is mitral incompetence as well

Aneurysmal dilatation of the left atrium is more common with mitral incompetence, but it can occur with pure stenosis The left atrial appendage may be enlarged disproportionately to the rest of the chamber in such cases there is a conspicuous bulge on the left border of the heart just below the pulmonary arc but little abnormal on the right border

*Heavy calcification of the mitral valve* implies considerable destruction of the valve mechanism and is therefore uncommon in cases of pure



Fig 10 1 —Skiagram showing the characteristic appearances of dilatation of the left atrium in the anterior view in a case of mitral stenosis



Fig 10 13—Skiagram in first oblique position showing enlarged left atrium delineated by means of barium in the œsophagus in a case of mitral stenosis

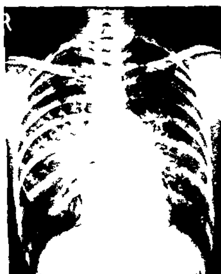


Fig 10 14—Skiagram from a case of tight mitral stenosis showing intense pulmonary venous congestion (probably chronic interstitial œdema) Horizontal Kerley lines can be seen in the right lower zone Dilatation of the pulmonary artery is due to passive pulmonary hypertension

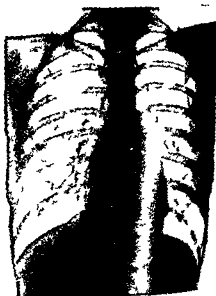
stenosis, on the other hand it does not necessarily mean that incompetence is dominant

*Pulmonary venous congestion* is supposed to be visible radiologically as fan shaped mottling in the hilar regions (fig 10 14) This traditional term has the advantage of familiarity but the disadvantage of inaccuracy, for the pulmonary veins are not in fact congested—if congested means over crowded—and the abnormal shadows are not venous The pulmonary venous pressure is certainly raised considerably in all cases having this radiological sign but the pulmonary veins themselves are constricted rather than dilated (Holling 1951) and the pulmonary blood volume is normal at rest (Lagerlof *et al* 1949) The precise nature of the hilar opacities awaits proof, but it is now believed that they are probably caused by a combination of chronic œdema and other changes in the interstitial connective tissue engorged lymphatics and dilated pleuro hilar bronchial veins These are the effects of pulmonary venous hypertension caused by impedance to flow the bottle neck being situated at the mitral orifice The radiological appearances themselves might well be called chronic interstitial œdema of the lungs

Horizontal linear markings best seen near the costophrenic angles usually accompany the hilar opacities (Kerley 1933 1936) These are believed to represent œdematous inter lobular septa (Grainger and Hearn 1955)



(a) 11th November 1942



(b) Two days later after medical treatment

Fig 10 15—Skiagram showing acute pulmonary œdema in a case of mitral stenosis

*(Acknowledgment to Sir John Parkinson)*

In mitral stenosis (and left ventricular failure) the degree of chronic interstitial œdema if this expression may be used is directly proportional to the height of the left atrial pressure and does not occur at all until the latter is over 10 mm Hg above the sternal angle at rest It is therefore proportional to the degree of stenosis and inversely proportional to the pulmonary vascular resistance.

*Acute pulmonary œdema* gives rise to a typical diffuse opacity spreading outwards from the hilum towards the periphery of the lung (fig 10 15) it is always bilateral but may be more conspicuous on one side than the other The œdema is intra alveolar and the shadows may develop and disappear within a matter of minutes or hours Attacks are more likely to occur in patients with previously normal lungs than in those who already have chronic interstitial œdema as explained earlier

*Pulmonary hæmosiderosis* is seen in 10 per cent of moderate or severe cases of mitral stenosis. Fine or coarse miliary nodules are scattered throughout the lungs (fig 10 16) and resemble those seen sometimes in certain hæmolytic anæmias of childhood (Gumpert 1947) The lesions are closely linked with repeated hæmoptysis and develop relatively early in the course of mitral stenosis at a time when hæmorrhages are common (Laubry Lenegre and Abbas, 1948) and the pulmonary vascular resistance



Fig 10 16—Skiagram of a case of mitral stenosis showing miliary nodules in the lungs due to hæmosiderosis



Fig 10 17—Skiagram showing considerable dilatation of the pulmonary artery in a case of mitral stenosis with an extreme pulmonary vascular resistance note the absence of chronic interstitial œdema of the lung

low (Wood, 1954) *The lesions represent focal accumulations of hæmosiderin in groups of adjacent alveoli with resulting fibrosis* (Lendrum 1950), *and are probably caused by hæmorrhages in the walls of the terminal* bronchioles secondary ossification occurs occasionally (Elkeles and Glynn, 1946) *Since hæmorrhages resulting from a rising pulmonary and bronchial* venous pressure tend to cease spontaneously, hæmosiderosis is never progressive beyond a certain point and since the lesions represent a permanent change of structure they never regress after successful valvotomy They have no greater significance than recurrent hæmoptysis and point unmistakably to past miliary hæmorrhages even when there has been no history of hæmoptysis

*Dilatation of the pulmonary artery* (fig 10 17) is due to pulmonary hypertension and its degree is proportional to the pulmonary vascular resistance (fig 10 18) Conspicuous dilatation of the pulmonary artery

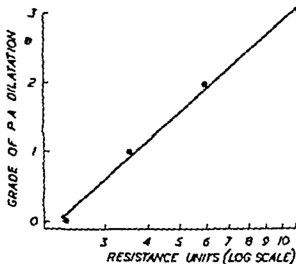



Fig 10 18—Graph showing the correlation between the radiological grade of pulmonary artery dilatation and the pulmonary vascular resistance (semi logarithmic scale)

*therefore provides good evidence of at least critical stenosis for a high resistance does not otherwise develop* Passive pulmonary hypertension *alone is rarely severe enough to have much effect on the pulmonary artery*

*Enlargement of the right ventricle* is more easily recognised clinically and *electrocardiographically than radiologically* but when the chamber responsible for cardiac enlargement has already been identified as the right ventricle by such means its actual size is best determined radiologically Like dilatation of the pulmonary artery the degree of right ventricular enlargement is proportional to the pulmonary vascular resistance and to

the duration of right ventricular failure when that has occurred Right sided enlargement is not a feature of simple mitral stenosis

*Dilatation of the right atrium* usually accompanies enlargement of the right ventricle and is difficult to distinguish from it by conventional radiological methods The combination of an inconspicuous pulmonary artery and dilated right heart suggests isolated enlargement of the right atrium due to tricuspid stenosis if the venous pulse and auscultatory signs deny such a diagnosis pericardial effusion should be seriously considered if that is excluded by means of cardiac catheterisation primary impairment of myocardial function due to fibrosis from old rheumatic carditis may have to be invoked although atrial fibrillation alone may be sufficient to explain some degree of dilatation

*General enlargement of the heart shadow* is rare in cases of mitral stenosis and when genuine is more likely to be caused by chronic pericardial effusion than rheumatic carditis or cardiac fibrosis As a rule however the statement that the heart is enlarged or that the cardio thoracic ratio is increased can be better expressed in terms of dilatation of the chamber or chambers responsible

*Angiocardiography* is of little value as a diagnostic tool in cases of mitral stenosis It helped however to prove that the hump on the left border of the heart between the pulmonary arc and left ventricle was the left atrium or left atrial appendage and not the conus of the right ventricle (Robb and Steinberg 1939 Grishman *et al* 1944) and that in cases with a high pulmonary vascular resistance the branches of the pulmonary arteries changed calibre abruptly and considerably instead of tapering off gradually (Davies *et al* 1953)

## PHYSIOLOGICAL TESTS

*Cardiac catheterisation* is now chiefly employed to measure the degree of stenosis when it is doubted whether the stricture is tight enough to explain the symptoms to determine whether mitral stenosis or incompetence is dominant in difficult borderline cases in which both are obviously present, to find out whether mitral stenosis is really responsible for a situation that is clinically indistinguishable from primary pulmonary hypertension or to discover whether pericardial effusion tricuspid stenosis or a myocardial fault is causing unexplained enlargement of the heart shadow

The degree of stenosis can be estimated by measuring the left atrial pressure the cardiac output and the heart rate A simple crude index of the size of the orifice is given by the ratio of the cardiac output (L / min ) to the left atrial pressure (mm Hg above the sternal angle) or C O /L A P Normally this is 5/5 or 100 per cent When mitral stenosis is trivial the index is still close to 100 per cent when the stricture is mild the index is about 5/10 or 50 per cent critical stenosis requiring valvotomy gives an average index of 4 5/22 5 or 20 per cent while with extreme stenosis th

index is about 3/25 or 12 per cent (Wood, 1954). For practical purposes this index works very well provided the heart rate does not exceed 90 beats per minute and there is no significant incompetence.

The size of the mitral orifice may be calculated more accurately by taking the heart rate into consideration for forward flow through the valve can only take place in diastole. According to the Gorlins (1951)

$$\text{mitral valve area} = \frac{\text{mitral flow in c.c. per second}}{31\sqrt{\text{L.A.P.} - \text{diastolic L.V.P. (mm. Hg)}}}$$

where mitral flow (c.c. per sec.) is $\dfrac{\text{cardiac output (c.c. per min.)}}{\text{diastolic filling period (sec. per min.)}}$

For example, in an average case of critical stenosis with a cardiac output of 4.5 litres per minute, a heart rate of 70 beats per minute and a left atrial pressure of 30 mm. Hg, the mitral flow in c.c. per second

would be $\dfrac{4.5 \times 1{,}000}{35\ \text{(approx.)}} = 128$, so that the mitral valve area would be

$$\frac{128}{31\sqrt{30-5\ \text{(assumed)}}} = 0.83\ \text{cm.}$$

Since the precise shape of the oval orifice is not known at operation it is impossible to determine its exact cross section when its length and breadth are estimated by a surgeon, but it is likely to be about two-third of the quotient, e.g. an orifice measuring 1 × 0.5 cm. should have a cross section of about 0.33 cm. A critical orifice measuring 0.83 cm. should have dimensions nearer 1.6 × 0.8 cm. Thus physiological calculations based on the Gorlin formula do not tally with Brock's estimates. This does not matter practically provided the order of the descrepancy is known.

Obstruction to forward flow may also be demonstrated by calculating the $R_{V/S}$ ratio from the left atrial pressure pulse, as explained on page 313. With severe critical and mild stenosis, the ratio averages 0.6, 1.0 and around 1.5 respectively. This test was introduced primarily to determine whether stenosis or incompetence was dominant in borderline cases in which both were known to be present: high ratios over 1.6 exclude obstruction to forward flow, so that under the clinical circumstances mitral incompetence can be diagnosed by inference.

The pulmonary vascular resistance in simple units is the pulmonary arterio-venous pressure gradient in mm. Hg divided by the cardiac output in litres per minute, as explained elsewhere. In 80 per cent of cases of mitral stenosis it is normal or only slightly raised, but in 12.5 per cent it lies between 6 and 10 units, and in 7.5 per cent between 10 and 30 units. Patients with an extreme pulmonary vascular resistance may resemble cases of primary pulmonary hypertension, but cardiac catheterisation always reveals a left atrial pressure over 10 mm. Hg with reference to the sternal angle, a stenotic index of 10 to 25 per cent, and an $R_{V/S}$ ratio under

1 3 The cardiac output is always low in these cases and the left atrial pressure strictly limited even when stenosis is extreme

The fourth reason for catheterising a case of mitral stenosis is to settle the question whether or not there is pericardial effusion, tricuspid stenosis or a myocardial fault, when apparent cardiac enlargement is otherwise unexplained

Pericardial effusion can at once be excluded if the tip of the catheter slides up and down the right border of the heart shadow when it is known to be in the right atrium If part of the heart shadow extends beyond the catheter tip as it lies against the lateral border of the right atrium however a dilated left atrium is as likely to be causing the opacity as pericardial effusion In either event dilatation of the right side of the heart without physiological cause is excluded

Tricuspid stenosis can be recognised at once if a continuous pressure tracing is recorded while the catheter is being withdrawn from the right ventricle to the right atrium for if there is any obstruction at the valve the right atrial diastolic pressure is appreciably higher than the right ventricular diastolic pressure (*vide infra*)

It is not so easy to demonstrate a myocardial fault Under routine conditions cases of primary myocardial failure associated with mitral stenosis should have a relatively low left atrial pressure perhaps 5 to 10 mm Hg above the sternal angle a more or less normal pulmonary arterio venous pressure gradient of 10 to 20 mm Hg raised right ventricular and right atrial diastolic pressures and a low cardiac output On exercise or on tipping head downwards the right ventricular and right atrial diastolic pressures should rise and the cardiac output should fall or at least fail to increase Cases that behave in this way are remarkably rare

Technically the left atrial pressure pulse on which most of the above calculations depend is recorded by wedging a catheter in a distal branch of the pulmonary artery, as described by Hellems *et al* (1948) and Lagerlof and Werko (1949) If this cannot be accomplished or if a satisfactory venous pulse is not so obtained the left atrial pressure may be measured directly by means of a needle inserted through the left bronchus (Allison and Linden, 1953), or through the chest wall posteriorly (Bjork *et al* 1953) Excellent tracings of the left atrial and left ventricular pressure pulses can of course be obtained at operation (fig 10 19)

*Respiratory function tests* may be required when the clinical features of a case suggest that cough and breathlessness may be due to chronic bronchitis and emphysema rather than to mitral stenosis When breathlessness is due to mitral stenosis the vital capacity and lung volume are reduced in proportion to the amount of chronic interstitial œdema present The residual volume mixing efficiency and poorly ventilated space are normal The maximum breathing capacity is diminished because of the mechanical difficulty in inflating and deflating the relatively rigid lungs the intra pleural pressure swings being greatly increased As a rule the blood gases

are normal, but in advanced cases with gross changes in the interstitial tissue there may be some difficulty in oxygen exchange as with diffuse pulmonary fibrosis The arterial oxygen saturation may then fall to 80 per cent, but rarely below this Elimination of carbon dioxide, which diffuses more readily than oxygen in a fluid medium is not hindered so that hyperventilation due to anoxia may be associated with a low arterial $pCO_2$ and carbon dioxide content

It will be appreciated that these findings at once distinguish the respiratory situation in mitral stenosis from that in *emphysema (q v) In* many respects however, they resemble the findings in diffuse interstitial fibrosis

The *pulmonary circulation time* is usually prolonged in well developed cases of mitral stenosis the delay being in the left atrium rather than in the pulmonary veins The test is therefore of little value because the dilated left atrium can be seen radiologically

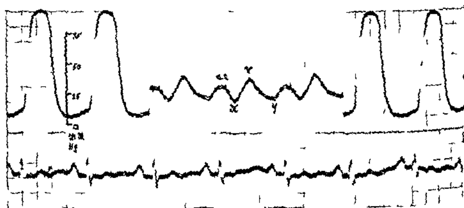


Fig 10 19 —Left ventricular and left atrial pressure pulses recorded in immediate succession from a case of mitral stenosis Note presystolic and diastolic pressure gradients across the mitral valve and the slow y descent following it

## COMPLICATIONS

Strictly speaking acute pulmonary œdema hæmoptysis winter bronchitis systemic embolism, laryngeal palsy and atrial fibrillation may all be regarded as complications of mitral stenosis but for convenience they have been treated as symptoms and have already been discussed There remain pulmonary hypertension pulmonary incompetence heart failure tricuspid incompetence pulmonary embolism bacterial endocarditis and massive thrombosis of the left atrium

*Pulmonary hypertension* may be active or passive The latter merely serves to keep the mean pulmonary artery pressure 10 mm Hg or so above the left atrial pressure and is clinically unimportant Active pulmonary hypertension implies a high pulmonary vascular resistance and a pulmonary arterio venous pressure gradient well above normal Two grades

of active pulmonary hypertension are recognised moderate with a pulmonary vascular resistance of 6 to 10 units and extreme with a pulmonary vascular resistance between 10 and 30 units

In my own series 28 per cent of 275 critical cases of mitral stenosis developed a high resistance moderate in 16 per cent and extreme in 12 per cent The change begins early, just as the degree of stricture is becoming critical High resistances are never encountered when stenosis is mild on the other hand extreme resistances may be encountered in young adults with only average stenosis (orifice 1 × 0 5 cm ) The available evidence favours the view that extreme resistances do not develop slowly over the years but relatively suddenly before pulmonary congestive symptoms have a chance to materialise It has already been explained that a high resistance protects the pulmonary venous system from developing dangerously high pressures and so prevents pulmonary œdema paroxysmal cardiac dyspnœa, and orthopnœa. On injecting 1 mg of acetylcholine into the pulmonary artery in these cases the pulmonary vascular resistance and pulmonary blood pressure fall the cardiac output rises and the left atrial pressure rises (Wood and Besterman 1956) In an ideal experiment the acetylcholine is totally inactivated before it reaches the systemic circulation and so far there has been no fall in systemic blood pressure on the contrary this has usually risen as a result of the increased output and there has been reflex cardiac slowing These results provide conclusive proof of the protective effect of pulmonary vasoconstriction on the pulmonary venous system in mitral stenosis and explain why high resistance cases do not suffer from pulmonary congestive symptoms In a carefully analysed series of 300 cases of mitral valve disease of all types 80 per cent of patients with an extreme pulmonary vascular resistance insisted that they had never had such symptoms Again if the high resistance were a late development it should be found more frequently in older patients in fact however the average age of patients with a high resistance is exactly the same as the mean age for all cases of mitral stenosis Finally, if a high resistance were due to sclerotic changes in the pulmonary arteries developing gradually over the years and secondary to passive pulmonary hypertension it should not be influenced by mitral valvotomy yet no case has so far been encountered in which the resistance did not fall appreciably after technically successful valvotomy

Just what causes the pulmonary vasoconstriction is unknown There is no experimental evidence that elevation of the pulmonary venous pressure *per se* has any such effect on the contrary the pulmonary artery pressure rises passively as it does in 80 per cent of cases of mitral stenosis Interstitial œdema can hardly excite the reflex for as previously explained these patients do not have such œdema and those that do usually have normal or only slightly raised resistances A reduced alveolar oxygen tension is known to cause pulmonary vasoconstriction but this does not occur

Clinically patients with an extreme pulmonary vascular resistance

usually present with fatigue, œdema angina pectoris or hæmoptysis from pulmonary infarction In other words the symptoms are those usually associated with a low cardiac output and not those associated with a high pulmonary venous pressure There is either a florid mitral facies and other evidence of intense peripheral vasoconstriction or rarely a palmar flush and signs of vasodilatation due to impairment of hepatic function The arterial pulse is exceptionally small The venous pressure is usually raised and the jugular pulse may show a giant *a* wave in cases with normal rhythm or a conspicuous v wave and deep y trough in cases with atrial fibrillation with or without functional tricuspid incompetence Occasionally, y may dominate the jugular pulse even when there is normal rhythm (fig 10 20)

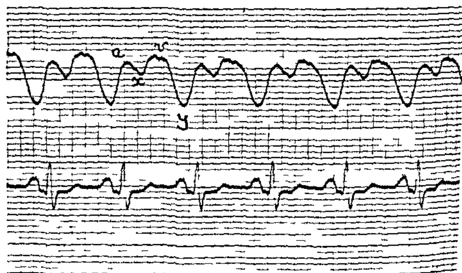



Fig 10 20—Jugular venous pulse tracing from a case of mitral stenosis with an extreme pulmonary vascular resistance and heart failure showing a rapid y descent and conspicuous y trough

The left ventricle is always impalpable but there is usually a substantial heave over the right ventricle which may extend to the left as far as the anterior axillary line occasionally there is a palpable impulse over the pulmonary artery The auscultatory signs of mitral stenosis are often greatly damped probably because the left ventricle through which they are ordinarily heard is unusually small displaced posteriorly and totally covered antero laterally by the enlarged right ventricle The mitral opening snap, however may be detected at the aortic area Right atrial gallop, a pulmonary ejection click accentuation of the pulmonary component of the second heart sound a pulmonary diastolic murmur due to functional pulmonary incompetence and a tricuspid systolic murmur due to func

tional tricuspid incompetence strongly confirms the diagnosis of severe pulmonary hypertension

The electrocardiogram shows a combined P pulmonale and P mitrale and considerable right ventricular preponderance X rays reveal conspicuous dilatation of the pulmonary artery and right side of the heart the pulmonary interstitial and vascular markings are relatively light and the left atrium may be only slightly dilated (fig 10 17)

The physiological findings include a giant *a* wave in the right atrial pressure pulse when there is normal rhythm or a conspicuous *v* wave followed by a sharp *y* descent and deep *y* trough in cases with atrial fibrillation a left atrial pressure pulse characteristic of at least critical stenosis a pulmonary artery pressure approaching but rarely exceeding

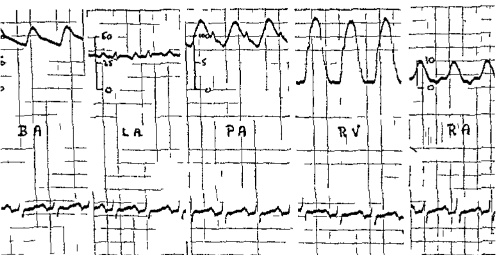



Fig 10 21—Pressure pulses from the brachial artery left atrium (indirect) and right side of the heart in a case of mitral stenosis with an extreme pulmonary vascular resistance The pulmonary artery pressure is higher than that in the brachial artery and a giant *a* wave is seen in the right atrial tracing

systemic level at rest (fig 10 21) a pulmonary arterio venous pressure gradient of some 30 to 70 mm Hg a high arterio venous oxygen difference associated with a low cardiac output and a pulmonary vascular resistance between 10 and 30 units (800 to 2 400 dynes sec /cm $^5$)

These high resistance cases sooner or later develop right ventricular failure, and are especially prone to phlebothrombosis in the legs with secondary pulmonary embolism which is often fatal

*Congestive heart failure*

It has been stated more than once that uncomplicated cases of mitral stenosis with normal rhythm or controlled atrial fibrillation do not develop heart failure although they may drown from pulmonary œdema The

complication above all others that causes failure is a high pulmonary vascular resistance Thus in a consecutive series of 200 cases of mitral stenosis in which the resistance was measured there was no single instance of heart failure when the resistance was less than 7 units excluding cases with uncontrolled atrial fibrillation When the resistance was 7 to 9 5 units 50 per cent of the cases failed and when it was 10 units or over 80 per cent failed (Wood 1954) It was concluded from these unexpected findings that active carditis residual myocardial fibrosis, or any other myocardial legacy from rheumatic fever could be dismissed as a practical cause for heart failure in cases of mitral stenosis Since then however it must be admitted that rare exceptions to this general rule have been discovered

The most dangerous precipitating cause of failure in these pulmonary hypertensive cases is pulmonary embolism secondary to phlebothrombosis in the legs

The most common cause of reversible heart failure in cases of mitral stenosis is uncontrolled atrial fibrillation The very rapid ventricular rate prevents adequate left ventricular filling the cardiac output falls precipitously the renal blood flow diminishes sodium is retained and hydræmia causes œdema and raises the venous pressure at the same time the left atrial pressure rises passive pulmonary hypertension may be considerable and if the resistance is moderately raised the right ventricle may be easily overloaded impairment of myocardial function secondary to an impoverished coronary blood flow adds to the difficulties Congestive heart failure brought about in this way is far less serious than that accompanying severe pulmonary hypertension and can be corrected rapidly by controlling the ventricular rate by means of digitalis

An upper respiratory tract infection has been identified as the chief precipitating factor in 45 per cent of cases of heart failure from mitral stenosis (Werner 1936) The effect may be due to tachycardia paroxysmal atrial fibrillation or a temporarily increased pulmonary vascular resistance

*Pulmonary embolism and infarction*

Late hæmoptysis is usually caused by pulmonary infarction and is commonly associated with incipient or actual heart failure in high resistance cases the infarct resulting from pulmonary embolism secondary to phlebothrombosis in the legs The low cardiac output raised venous pressure and immobilisation all encourage phlebothrombosis Emboli are often recurrent, and by obstructing part of the pulmonary arterial tree increase the total pulmonary vascular resistance, so that heart failure increases and a vicious circle is established Pulmonary embolism is the commonest cause of death in this type of case Pulmonary infarction may also result from pulmonary arterial thrombosis in cases of long standing pulmonary hypertension but this is believed to be relatively rare

*Pulmonary incompetence*

Functional pulmonary incompetence in cases of mitral stenosis always

means a high pulmonary vascular resistance and considerable dilatation of the pulmonary artery A basal diastolic murmur associated with a relatively normal pulmonary artery and normal resistance may be safely assumed to be aortic in origin even when there is no other evidence of aortic incompetence

*Tricuspid incompetence*

Functional tricuspid incompetence always means considerable dilatation of the right ventricle and in cases of mitral stenosis implies a high pulmonary vascular resistance The leak is usually reversible The physical signs include a diminished x descent high amplitude v wave rapid y descent and deep y trough in the jugular pulse systolic pulsation of the liver and a pan systolic murmur waxing on inspiration in the tricuspid area In view of the great dilatation of the right ventricle in these cases the tricuspid murmur may be very well heard at the apex beat and may then be mistaken for the murmur of mitral incompetence

If the pulmonary vascular resistance is not high tricuspid incompetence should be regarded as organic and careful re examination is likely to disclose some evidence of stenosis for organic tricuspid lesions are rarely purely incompetent

*Bacterial endocarditis*

It is unusual for bacterial endocarditis to complicate established cases of mitral stenosis and only one example has been seen by the writer while studying over 500 cases of mitral valve disease during the past seven years When bacterial endocarditis involves the mitral valve the latter is nearly always incompetent

*Massive thrombosis of the left atrium*

Massive thrombosis occupying more than half of the left atrial cavity may be firmly adherent pedunculated or entirely free It occurs in about 2 per cent of cases of mitral stenosis (Garvin 1941) and is usually associated with atrial fibrillation The left atrium shows no special features to account for the size of the clot Free or pedunculated ball valve thrombi may block the mitral orifice and virtually halt the circulation causing sudden death or partial obstruction may result in syncope loss of peripheral pulses and severe symmetrical ischæmia of the extremities ears and tip of the nose as emphasised by Fishberg (1940) More often however the symptoms of massive thrombosis do not differ qualitatively from those of uncomplicated mitral stenosis but they may develop suddenly and tend to be severe Angina pectoris was stressed by Evans and Benson (1948) and may be attributed to the unusually low output It was hoped that angiocardiography might reveal an obvious filling defect of the left atrium in cases of massive thrombosis as it may experimentally in dogs (Read *et al* 1955) but the clot has proved difficult to demonstrate by these or other pre operative means

*ASSOCIATED CONDITIONS*

*Pregnancy* One of the most important events in the life history of a woman with mitral stenosis is pregnancy The subject is discussed in detail elsewhere It may be noted here however, that one third of all pregnancies in cases of mitral stenosis cause temporary (44 per cent) or permanent (56 per cent) deterioration The chief symptoms are cough dyspnœa hæmoptysis orthopnœa paroxysmal dyspnœa and acute pulmonary œdema atrial fibrillation systemic embolism and congestive failure are relatively rare When symptoms develop they usually begin before the end of the first trimester This tallies with physiological evidence that hydræmia and a moderate increase of cardiac output occur quite early in pregnancy, and can be demonstrated regularly during the third month (Burwell *et al* 1938 Palmer and Walker, 1949)

*Anæmia* usually due to iron deficiency may precipitate ' congestive symptoms in much the same way as pregnancy the raised cardiac output being responsible In practice the hæmoglobin is below 60 per cent and usually below 50 per cent before the output is sufficiently increased to raise the pulmonary venous pressure Before advising valvotomy therefore it is wise to check the hæmoglobin for symptoms may disappear after an iron deficiency anæmia is corrected

*Thyrotoxicosis* aggravates the effects of mitral stenosis by causing tachycardia and a raised cardiac output both of which are poorly tolerated as previously explained The hyperthyroidism should be corrected medically before attempting to assess the severity of the mitral stenosis if the latter requires valvotomy there is a good case for treating the goitre first by means of radio active iodine if the stricture is relatively mild the physician is at liberty to treat the thyrotoxicosis by any of the accepted methods that might seem most suitable on other grounds

*Active rheumatic carditis* is present in at least one third of relatively severe cases of mitral stenosis if Aschoff nodes in biopsy and post mortem material may be so interpreted The activity however is very low grade and rarely seems to influence the behaviour of the heart muscle whether or not it has any bearing on the rate at which stenosis develops or increases however is a moot point Very occasionally unexplained dilatation of the heart associated with a low cardiac output left atrial pressure under 10 mm Hg and relatively normal pulmonary vascular resistance suggests serious myocarditis or myocardial fibrosis but proof is lacking In children with established mitral stenosis there is no doubt that a recurrence of active carditis may cause reversible heart failure but fever, tachycardia and other hæmodynamic changes may be partly responsible Considering the frequency of mitral stenosis it is quite likely that some cases of unexplained heart failure associated with a relatively mild stricture are due to non rheumatic coincidental myocarditis of the type described by Gore and Sapphir (1947)

*Rheumatoid arthritis* may be associated with mitral stenosis and may be

mistaken for a recurrence of rheumatic fever The chief cardiac complication of rheumatoid is pericarditis but a specific myocardial lesion occurs in about 2 per cent (Sokoloff 1953) Mitral valve disease is never due to rheumatoid itself

*Chronic pulmonary tuberculosis* occurs in about 2 per cent of cases which is the same as in the general population There is no evidence that the congested lung of mitral stenosis is antagonistic to tuberculosis

*Bronchitis and emphysema* have already been discussed Very rarely severe emphysema or *interstitial pulmonary fibrosis* may be incidentally associated with mitral stenosis and may be primarily responsible for breathlessness Both should be carefully considered when dyspnœa seems disproportionate to the estimated degree of stenosis It should be borne in mind that emphysema masks the auscultatory signs of mitral stenosis that rhonci may well be due to œdematous bronchial mucosa secondary to mitral stenosis, that the radiological appearances of interstitial pulmonary fibrosis can be very similar to those of chronic interstitial pulmonary œdema and that pulmonary physiology in these last two conditions can also be alike If there is any doubt about what is causing the breathlessness appropriate lung function tests should be carried out and the size of the mitral orifice calculated from data obtained at cardiac catheterisation for mistakes are certainly being made both ways patients with severe mitral stenosis being left to die in the belief that they are suffering from advanced emphysema and patients with severe interstitial pulmonary fibrosis being operated on for relatively mild mitral stenosis under the false impression that the latter is causing the dyspnœa

*Essential hypertension* (blood pressure 160/100 or above) occurred in only 3 per cent of the author s series and the diastolic pressure was as high as 120 mm Hg in only 1 per cent Conversely Bechgaard (1946) found that only 1 per cent of cases of essential hypertension had mitral stenosis Following valvotomy any tendency towards hypertension may become more evident

*Congenital anomalies* sometimes associated with congenital or acquired mitral stenosis include coarctation of the aorta patent ductus arteriosus and atrial septal defect The effects of such combined lesions on the physiology of the circulation have already been described in chapter VIII Since all are now repairable double operations may be performed if necessary

## *DIFFERENTIAL DIAGNOSIS*

There is rarely much difficulty in recognising a case of mitral stenosis unless the characteristic physical signs are masked by a huge right ventricle or considerable emphysema the diagnostic problem is more concerned with the degree of stricture the amount of incompetence (if any) the height of the pulmonary vascular resistance the state of the myocardium the nature and degree of other valve lesions the state of the lungs and the

presence or absence of the various complications or associated conditions enumerated and discussed above No object would be achieved by commenting further on any of these things

## *COURSE AND PROGNOSIS*

The course of mitral stenosis may be summarised here with advantage The initial rheumatic attack usually occurs between the ages of 8 and 1. The worst cases die within five years, the mortality in the active phase of the disease being 6 5 per cent The vast majority of those that recover become temporarily free from symptoms although some patients limit their activities on medical advice and others have a psychologically induced effort syndrome

The symptom free period lasts for an average of about 20 years Approximately the first half of this period is occupied with the development of physiological stenosis and is therefore a true latent interval in the second half mitral stenosis can be readily detected but the stricture is too mild to cause any symptoms Around the age of 30 true effort dyspnœa develops and usually increases a grade every 2 to 3 years so that total incapcity is reached in 7 to 8 years The steps in this relentless deterioration often appear to be sudden being precipitated by pregnancy influenza winter bronchitis the onset of atrial fibrillation a period of excessive worry or hard work or some such factor The course may also be punctuated by recurrent hæmoptysis systemic embolism acute pulmonary œdema severe bronchitis or paroxysmal atrial fibrillation

A proportion of patients die prematurely from hemiplegia or acute pulmonary œdema The development of structural changes in the interstitial tissue of the lungs helps to prolong life by allowing high left atrial pressures to be built up with relatively little danger of pulmonary œdema and the development of a high pulmonary vascular resistance may prolong life by preventing the build up of dangerously high left atrial pressures but at the expense of a low cardiac output and ultimate heart failure Patients in the first group tend to die in an attack of acute bronchitis or bronchopneumonia and those in the second group from heart failure often aggravated or precipitated by phlebothrombosis and pulmonary embolism The average duration of total incapacity is about three years so that the total period of symptoms occupies about ten years and the average age of death is about 40 There is of course a very wide variation in behaviour from case to case some patients dying in adolescence others reaching old age The figures given indicate a better prognosis than in the series reported by De Graff and Lingg (1935) in which the average age of death was 29 for cases with normal rhythm and 38 for cases with atrial fibrillation and a worse prognosis than in the follow up series analysed by Olesen (1955) in which the average age of death was 47 and the interval between the onset of symptoms and total incapacity was 15 years

## TREATMENT

The management and treatment of cases of mitral stenosis is a joint concern being partly medical and partly surgical All agree theoretically that this should be so but in practice there is a growing tendency for the physician s part to be dismissed as unnecessary and time wasting so that more and more patients are being sent direct to surgical clinics It is imperative that this tendency be halted abruptly and permanently for th total physiological disturbance that results from mitral valve disease is very much a medical problem it is often thoroughly complicated and proper selection of cases for surgical treatment demands a physician s knowledge training and skill moreover there is a great deal more in the management of cases of mitral stenosis than surgical relief of the stricture fundamental and epoch making though the latter may be The physician s therapeutic responsibilities include governing the patient s total activitie steering a woman through or away from pregnancy recognising and treating important coincidental conditions such as psycho neurosis anæmia and thyrotoxicosis managing recurrent hæmoptysis preventing and treating paroxysmal cardiac dyspnœa and acute pulmonary œdema respecting and treating attacks of winter bronchitis controlling the rhythm preventing systemic and pulmonary embolism as far as possible appreciating the cause of heart failure and improving the circulation as much as possible selecting cases that require valvotomy and preparing them for the operation restoring normal rhythm post operatively accurately assessing the physio logical situation three months later and guiding the patient in the most advantageous way for the rest of his medically eventful life for valvotomy does not cure rheumatic heart disease The outstanding aims of medical research workers in this field must be to prevent rheumatic fever to prevent or cure active endocarditis or at least to prevent fusion of the cusps

The patient s *work and other activities* should be regulated in accordance with the expected life history of the lesion If there is no detectable stenosis or no more than a trivial mitral leak 10 to 15 years after the initial rheumatic attack the patient should be encouraged to lead an entirely normal life If on the other hand stenosis can be detected at this time even though trivial in degree the patient should be advised to take up an occupation that will never involve him in more than light physical work so that when symptoms develop he will not have to retire During the symptom free period ordinary physical activities including all but the most strenuous competitive sports such as rowing and long distance running should be allowed on the other hand such patients must be rejected for national service and are likely to be rejected or heavily loaded by life insurance companies A woman wanting to have a family should take advantage of this latent period in which to complete it for it may be her last safe *opportunity* to do so At the average age of 30 or so grade 1 effort intolerance develops and progresses to grade 2A over a variable time averaging about three years During this period patients should be encouraged to continue all activities

that do not cause dyspnœa but to avoid those that do If their occupations have been chosen wisely they should have no difficulty in continuing with their work free from breathlessness Any further deterioration usually means that dyspnœa is beginning to interfere seriously with the patient s happiness and comfort and the time for valvotomy has arrived

*Pregnancy* precipitates or aggravates symptoms in one third of cases the deterioration being permanent in half of them If the valve lesion is obviously amenable to surgical treatment a woman with grade 1 or 2A effort intolerance should not be advised against pregnancy if she is willing to have the operation should the necessity arise If symptoms are not aggravated all is well If she deteriorates seriously she usually begins to do so in the third month and valvotomy can then be carried out if necessary the pregnancy being allowed to continue to term If the patient starts pregnancy with only grade 1 effort intolerance any exaccerbation of symptoms can usually be controlled by medical means and valvotomy is better deferred patients starting pregnancy with grade 2A effort intolerance are more likely to cause anxiety and may well require valvotomy during the second trimester Women with grade 2B effort intolerance should be advised against pregnancy unless valvotomy is carried out first if they are already pregnant valvotomy should be advised without delay If the nature of the valve lesion is such as to make surgical relief impracticable women with more than slight effort intolerance should be advised against pregnancy and preferably sterilised If she has already conceived the pregnancy is best terminated during the first three or four months by therapeutic abortion or hysterectomy if she is already five or six months pregnant and her life is not in imminent danger she can usually be taken through to term and delivered naturally symptoms being controlled by rest and appropriate medical measures Urgent hysterotomy is rarely necessary or desirable

*Coincidental psycho neurosis* may be entirely responsible for any disability in cases of mitral stenosis the symptoms being wholly psychosomatic or it may encourage pulmonary congestive symptoms by raising the cardiac output and heart rate This is an important diagnostic problem which must be solved correctly Effective psychotherapy is as important as curing anæmia or controlling thyrotoxicosis and should be undertaken before advising valvotomy

*Coincidental anæmia* may be spontaneous or secondary to repeated hæmoptysis usually the former Iron deficiency is commonly responsible and replacement therapy rapidly effective Transfusion is rarely required but packed cells may be given slowly if necessary Intravenous infusions of any kind are highly dangerous in mitral stenosis

*Coincidental thyrotoxicosis* is probably best treated by means of radio active iodine Mitral valvotomy can then be undertaken later if necessary Partial thyroidectomy is not without added risk in the presence of tight mitral stenosis and antithyroid drugs are unlikely to be satisfactory in the

long run In view of the bad effect of a raised cardiac output on ... mitral valve disease it is imperative that the thyrotoxicosis should properly and permanently controlled

*Suspected or proved rheumatic activity* should be allowed to settle d before advising valvotomy when the latter is indicated but the operation should not be deferred if it is urgent There is no convincing evidence that cortisone improves the carditis or diminishes the operation risk

*Hæmoptysis* from rupture of a broncho pulmonary venous radicle usually ceases spontaneously within a few hours If it is severe or repetitive it may be wise to lower the pulmonary venous pressure by means of rest posture mersalyl and a low sodium diet The patient should be reassured that these hæmorrhages are not serious occur relatively early in the course of mitral stenosis are not in themselves an indication for valvotomy and tend not to recur after certain natural adjustments to the circulation have taken place

*Acute pulmonary œdema* is a medical emergency but it is not a surgical emergency The patient should be treated sitting bolt upright with the legs down Venous tourniquets should be applied to the thighs as high up as possible Morphine gr ¼ or pethidine 100 mg should be injected intra muscularly The chief object of these measures is to lower the right ventricular output and so reduce the pulmonary venous pressure Powerful sedatives may also have some indirect influence on the permeability of the pulmonary capillaries Aminophylline 0 24 G intravenously may help by relieving bronchospasm Oxygen administered through a simple light plastic mask may help to correct the falling arterial oxygen tension and counteract the adverse effect of anoxia on the pulmonary capillary permea bility whether or not anoxia helps to bring the attack to an end by causing pulmonary vasoconstriction is not yet known for certain but a fall in alveolar oxygen tension is known to have this effect and oxygen may yet prove to be a two edged weapon

If the patient does not improve a suction catheter should be passed down the trachea via the nose or mouth in order to clear the air passages or if facilities are available bronchoscopic suction may be employed This may be life saving when a patient is drowning in fluid which is filling the air passages Finally venesection should not be unduly delayed if the occasion seems to demand it about a pint of blood should be removed

Acute pulmonary œdema can usually be prevented when its imminence is recognised by limiting physical and emotional activities (sexual inter course is a common precipitating agent) and prescribing a low sodium diet mercurial diuretics and sedatives Patients should sleep well propped up at night Respiratory infections should be treated promptly in these dangerous cases for they too may precipitate an attack Paroxysmal atrial fibrillation with a rapid ventricular rate may also be responsible and if this is suspected digitalis should be given

When the situation is under good medical control but not before valvotomy should be performed It has been well said that the patient

should not be allowed to leave hospital until the stricture has been relieved (Baker *et al* 1952)

*Paroxysmal cardiac dyspnœa* in which the exudation from the capillaries does not extend beyond the interstitial tissues calls for the same remedial and prophylactic treatment as acute pulmonary œdema except that intra tracheal suction is never indicated

*Acute bronchitis* deserves considerable respect for attacks are accom panied by much discomfort and dyspnœa and blood spitting may add to the patient s alarm Antibiotics should be supported by strong measures designed to lower the bronchial venous pressure e g posture and mercurial diuretics a low sodium diet and strict control of the ventricular rate by means of digitalis in cases with atrial fibrillation Aminophylline helps to relieve bronchospasm

*The onset of paroxysmal or permanent atrial fibrillation* is usually accom panied by a very rapid ventricular rate which in cases of mitral stenosis may have serious consequences as previously explained The chief dangers are acute pulmonary œdema congestive heart failure and cerebral embo lism The onset of atrial fibrillation in mitral stenosis should therefore be regarded as a medical emergency and should be treated promptly with digitalis heparin and dehydration until the ventricular rate is controlled The object of the heparin is to prevent left atrial thrombosis and 15 000 units should be given intravenously in the first instance, followed by similar doses two or three times daily intravenously or intramuscularly until digitalis is having the desired effect Prophylactic dehydration by means of mercurial diuretics and a fruit and rice diet for 48 hours help to prevent pulmonary œdema and heart failure If the patient happens to be in hospital at the time and therefore under constant supervision it may be best to give digoxin intravenously in an initial dose of 1 mg followed by 0 5 mg two hourly until the ventricular rate is under 100 beats per minute after which injections should be replaced by an oral maintenance dose A single injection of heparin intravenously and 2 ml of mersalyl intramuscularly should then suffice for the ventricular rate should be controlled within six hours If acute pulmonary œdema is present or threatened when the patient is first seen the initial intravenous dose of digoxin may be 1 5 mg but on no account more than this and subsequent doses must never exceed 0 5 mg

*Permanent atrial fibrillation* is best treated with a maintenance dose of digitalis attempts to restore and maintain normal rhythm being rarely worth while prior to valvotomy The matter is discussed more fully in chapter VI

*Systemic embolism* is due to liberation of a fresh clot from the left atrium and though usually unpredictable a limited number undoubtedly occur within a few days following the onset of atrial fibrillation with rapid ven tricular rate and these could probably be prevented by means of heparin if the danger were more widely recognised Emboli are often recurrent and

in view of their serious consequences there is something to be said in favour of treating all embolic cases with dindevan until valvotomy is performed or for life if for any reason valvotomy is contra indicated. Embolism bears little relation to the degree of mitral stricture as previously pointed out but its occurrence in otherwise uncomplicated mitral stenosis is usually sufficient reason for advising valvotomy unless the mitral index is over 45 per cent Treatment of the embolism is discussed in chapter I

*Pulmonary embolism* is a late manifestation of a retarded circulation in cases with a high pulmonary vascular resistance and actual or incipient heart failure In my own series this was the commonest cause of death in cases of mitral stenosis partly because the danger was not at first recognised Since treating all severe pulmonary hypertensive cases with dindevan until mitral valvotomy was carried out there have been no further deaths from this source over a period of nearly three years Prior to the adoption of this policy seven out of eight medical deaths from mitral stenosis were due to pulmonary embolism six of them in high resistance cases (Wood 1954) During the same period there was only one death from acute pulmonary œdema and that was partly the result of bronchopneumonia

If pulmonary embolism has already occurred 15 000 units of heparin should be given at once intravenously followed by adequate anticoagulant treatment for the danger of further phlebothrombosis is imminent and any delay in preventing it may be lethal There need be no fear that anticoagulants may cause serious hæmorrhage from a pulmonary infarct although hæmoptysis may be rather more prolonged The risk with which we are concerned is not hæmorrhage from an infarct but obstruction of the pulmonary circulation from recurrent embolism If mitral valvotomy cannot be carried out in this type of case because there is too much mitral incompetence the patient is too old or the operation is refused then permanent anticoagulant therapy should probably be advised

The immediate treatment of massive pulmonary embolism also includes nursing the patient flat oxygen respiratory stimulants such as aminophylline or coramine and digitalis as described in chapter XVII

*Heart failure* calls for complete rest preferably in a cardiac bed digitalis mercurial diuretics and a low sodium diet as detailed in chapter VII In cases of mitral stenosis it is especially important to identify the cause of the failure for it is far from being an inevitable consequence of the valve lesion The only two common causes are uncontrolled atrial fibrillation and a high pulmonary vascular resistance With the former rapid recovery follows adequate doses of digitalis alone and the subsequent outlook may then be quite good the latter is much more serious and improvement can only be temporary unless mitral valvotomy is performed

## *MITRAL VALVOTOMY*

The treatment of mitral stenosis has been radically altered since the introduction of mitral valvotomy by Harken (1948) and Bailey (1949) in

the United States and independently by Brock (Baker Brock and Campbell 1950) in England It is true that Souttar performed the first successful digital mitral valvotomy as early as 1925 but the operation did not gain favour at that time perhaps because it was then believed that the myocardium was primarily at fault and the valve lesion relatively unimportant at that time too thoracic surgery was a formidable undertaking anæsthesia was far less advanced there were no antibiotics and there was little to encourage cardiac surgery of any kind In 1948 however the situation was radically different and mitral valvotomy was instantly acclaimed Since then thousands of cases of mitral stenosis have been relieved of their stricture and parallel physiological studies have placed the operation on a firm scientific footing The easiest and best approach is through the left atrial appendage In the simplest cases the fused commissures are separated digitally and the split is continued as far as the ring on both sides More often dense cross fusion at the critical areas of tendinous insertion have to be cut with a special knife Sometimes only one commissure can be split and occasionally the architecture of the valve is so deranged that little can be done Heavy calcification may also interfere with the operation particularly on the medial side but not necessarily Clots in the left atrium can usually be recognised by the surgeon and may often be washed out by allowing a brief frank hæmorrhage to take place through the atrial appendix a second precaution is to place tapes behind the common carotid arteries so that these vessels may be occluded for a few vital seconds when there is any danger of embolism For proper surgical details however the reader must consult appropriate surgical works

*Selection of cases for valvotomy*

In general any patient who is *suffering* from the effects of mitral *stenosis* requires valvotomy and any patient who is able to continue his normal occupation without distress does not There are several reasons for not operating prematurely (1) the surgical mortality in relatively mild uncomplicated cases is not negligible (1 7 per cent in my own series) (2) the risk of cerebral embolism at operation is not confined to advanced cases (3) a technically good result is only achieved in 75 per cent of cases and is no more likely when the stricture is relatively mild than when it is extreme (4) there is little doubt that post operative re stenosis is going to prove troublesome for it is already occurring at the rate of about 2 per cent per annum and second valvotomies are proving more difficult than the first The chief dangers of waiting until effort intolerance is grade 2B are cerebral embolism and acute pulmonary œdema, both of which may occur unexpectedly in relatively mild cases

Any patient then with simple mitral stenosis and grade 2B or greater effort intolerance should be advised to have the stricture relieved The following remarks summarise briefly the various modifying factors that have been discussed in detail previously

*Age* Patients under 20 years old should be deferred as long as possible in view of the likelihood of activity and the presumed greater risk of re stenosis patients in the sixth decade on the other hand should not be deferred too long for they may soon be too old for the operation

*Rheumatic activity* is obviously adverse but is not a contra indication if life is threatened by the stricture

*Recurrent bronchitis* should encourage valvotomy for it is usually the result of a high bronchial venous pressure Secondary emphysema is rarely severe enough to prevent a successful outcome

*Systemic embolism* is the one complication that demands valvotomy at a time that would be regarded as premature on other grounds

*Hæmoptysis* even when recurrent and profuse rarely provides sufficient reason for surgical intervention

*Acute pulmonary œdema* provides the strongest grounds for advising valvotomy as soon as intensive medical treatment has brought the situation under control

A *high pulmonary vascular resistance* may mask the severity of mitral stenosis by inhibiting pulmonary venous congestion Since the resistance is never raised unless the stenosis is at least critical valvotomy should be undertaken in all such cases When the resistance is extreme the matter is urgent owing to the grave danger of heart failure and pulmonary embolism

*Atrial fibrillation* has no direct bearing on the question of surgery but if it has been associated with a rapid ventricular rate breathlessness and œdema may give a false impression of the severity of the stenosis and an operation may have been advised when only digitalis is needed

*Of the physical signs* of uncomplicated mitral stenosis only the brevity of the interval between the aortic second sound and the opening snap and the length of the mitral diastolic murmur give any indication of the severity of the lesion The louder and sharper the first sound and the opening snap the more mobile are the mitral cusps and in such cases a good technical result may be expected from valvotomy (Sellors Bedford and Somerville 1953) Damping of the first sound and absence of the snap are usually due to heavy calcification but this should not prevent a successful outcome although only one commissure may be split

The *electrocardiogram* should show an obvious P mitrale in any case severe enough to warrant valvotomy provided the rhythm is normal Right ventricular preponderance judged by the appearances in multiple chest leads means a high pulmonary vascular resistance and therefore indicates surgical treatment

*X rays* are particularly helpful in showing the amount of chronic interstitial œdema present for this is closely related to the pulmonary venous pressure and therefore to the degree of stricture Radiological evidence of pulmonary hypertension emphasises the need for valvotomy it should be remembered that in these cases signs of pulmonary venous congestion may be absent

*Cardiac catheterisation* should reveal a left atrial pressure well over 10 mm Hg with reference to the sternal angle a mitral stenotic index not exceeding 33 per cent and an Ry/v ratio not exceeding 1 5 average figures for surgical cases are 22 mm Hg 15 to 20 per cent and 0 8 to 1 0 respectively A high pulmonary vascular resistance, which in case of mitral stenosis always indicates valvotomy means that the pulmonary arterio venous pressure gradient is at least 30 mm Hg and the gradient divided by the cardiac output in litres per minute is at least 6 and in extreme cases at least 10 If the Gorlin formula is used the critical mitral orifice is 1 cm $^2$

*The chief difficulties in selecting cases* for valvotomy however usually have less to do with the criteria and modifying factors just enumerated than with estimating the significance and degree of other valve lesions especially mitral incompetence To discuss the effect of other valve lesions on the varying physiology of mitral stenosis would entail too much repetition to be profitable for the possible permutations and combinations are almost endless Considerable experience is necessary to appreciate just what is going on in some of these complicated cases and the decision to advise or withhold mitral valvotomy can be very difficult

*Pre operative treatment*

Medical measures designed to diminish the operative risk and post operative complications include rest and sedatives digitalis dehydration anticoagulants and treatment of bronchitis

Rest and sedatives are advisable for a few days beforehand while the total situation is being reviewed but if unduly prolonged merely add to the patient s anxiety

*Digitalis* should be given as a routine whether there is normal *rhythm* or otherwise so that a rapid ventricular rate does not accompany post operative atrial fibrillation should that occur It is wise to start digitalis two or three weeks before valvotomy is planned so that the right maintenance dose is arrived at in good time This is not easily determined in cases with normal rhythm free from heart failure It may be best to start with tabs dig *folia* gr 2 t d s *for two days followed by* gr 1 t d s *for* two days followed by gr 1 twice daily thereafter This should prove sufficient in most cases and rarely too much If nausea develops the maintenance dose should be reduced to gr ½ t d s or 0 1 mg of digitoxin daily which is its equivalent When there is atrial fibrillation the ventricular rate must be properly controlled before valvotomy

Quinidine is not advised It has failed to prevent post operative atrial fibrillation and unless full doses of digitalis are also given it then encourages a more rapid ventricular rate slowing down the speed of the f waves so that the ventricles try to keep pace

*Dehydration* by means of mercurial diuretics and a low sodium diet supported or not with resins or diamox should be strictly enforced in all cases liable to acute pulmonary œdema or paroxysmal dyspnœa in all

orthopnœa cases when X rays show considerable interstitial hilar mottling and when there is heart failure secondary to a high pulmonary vascular resistance but not otherwise

*Anticoagulants* have already been discussed in relation to cases with an extreme pulmonary vascular resistance or recurrent systemic embolism Dicoumarol tromexan or dindevan is usually withheld four or five days before the operation

*Bronchitis* should be improved as much as possible before valvotomy This may mean a course of some suitable antibiotic—penicillin if the organism is believed to be the pneumococcus streptomycin if H influenzæ is responsible (May 1953)—in addition to dehydration (to lower the bronchial venous pressure) and antispasmodics such as aminophylline

Valvotomy should be deferred for several months following *hemiplegia* in view of the grave risk of post operative pulmonary complications in these cases

*Post operative course and management*

Immediate post operative management is a surgical responsibility and includes treatment of shock peripheral embolism hæmorrhage collapse of the lungs attending to pleural drainage and regulating fluid balance The comments made here are confined to the more medical aspects of the case

*Hemiplegia* occurs in about 5 per cent of cases and is always due to cerebral embolism at the time of the operation although it may not be discovered until the patient regains consciousness Subsequent embolism is extremely rare There is no effective treatment for embolic hemiplegia but spontaneous improvement may be rapid and considerable

*Aortic saddle embolism* or high femoral embolism is usually detected immediately if it occurs during the operation because checking all peripheral pulses is part of the surgical routine Embolectomy is always best carried out then and there

*Post operative psychosis* may be attributable to prolonged cardiac stand still or ventricular fibrillation during the valvotomy or to hepatic failure in patients who have had prolonged heart failure The first type is usually represented by a quietly confused soporific or comatose state the second by violently aggressive abusive or paranoid behaviour Both are serious in that they represent considerable functional damage to the cerebral cortex and liver respectively As a rule recovery is complete within a few weeks but a minority lapse into coma and death Little can be done to influence the issue

*Chest complications* include hæmothorax pleural effusion collapse of the lung and bronchitis or bronchopneumonia They usually settle down satisfactorily with appropriate treatment

*Post operative atrial fibrillation* occurs in one quarter of the cases w

previously normal rhythm This is not prevented by quinidine but causes little disturbance if prophylactic digitalis has been given It usually develops between the second and fifth day and if left to nature stops spontaneously after an average of ten days in about half the cases, and becomes permanent in the other half Attempts to restore normal rhythm at once usually fail the natural course of events indicates that quinidine should be withheld until the end of the second post operative week and if given then proves successful in 95 per cent of cases in which the valvotomy has been technically successful (Wood 1954)

Normal rhythm can also be restored in 50 per cent of patients with established pre operative atrial fibrillation but can only be maintained for long in three fifths of these

If the initial attempt to restore normal rhythm fails a second attempt may be made a few weeks later but usually without lasting success

The chief contra indications to quinidine therapy include technically unsuccessful valvotomy too much mitral incompetence extensive left atrial thrombosis and grossly diseased left atrial muscle found at operation The most important additional factor militating against prolonged maintenance of normal rhythm is advancing age

*Traumatic pericarditis* is believed to be responsible for the recurrent attacks of left chest pain and fever that punctuate the post operative course in 10 per cent of cases (Wood 1954) The pain is pericardial in behaviour and distribution there may be pericardial friction or radiological evidence of effusion there are often electrocardiographic changes compatible with pericarditis The fever lasts about a week and subsides without treatment After an interval of two or three weeks a second attack may occur and then perhaps a third or even a fourth Sooner or later the attacks cease for good and leave no sequelæ they are not dangerous but may interfere considerably with convalescence Similar episodes occur when a bullet or piece of shrapnel is lying in or close to the pericardium and have also been observed following direct cardiac surgery in cases of pulmonary stenosis

*Heart failure* following mitral valvotomy may be due to post operative sodium retention or chloride deficiency to increased mitral incompetence or to uncontrolled atrial fibrillation An increase of pulmonary venous congestion is nearly always due to the unfortunate development of considerable mitral incompetence which is one of the risks of surgical treatment Convalescence should be very slow in these cases to give the left ventricle time to adjust itself to the changed conditions Should signs of "heart failure develop with normal serum electrolytes normal rhythm controlled atrial fibrillation and no mitral incompetence pericardial effusion should be excluded before blaming the myocardium A rare cause of post operative heart failure is pulmonary embolism

Patients are usually allowed to get up during the second week as soon as their condition warrants it and if there are no complications they may be discharged from hospital during the third week but they should remain

under close medical supervision for three months if possible and should be warned of the possibility of recurrent pericarditis

*Results*

In the first 260 patients operated on at the Brompton Hospital 6·9 per cent died. The results were excellent in 30 per cent, good in 40 per cent, fair in 15 per cent and poor in 8 per cent. The best cases became symptom free or, if previously totally incapacitated, improved to the extent of having only slight effort intolerance. In other words, effort intolerance changed by three grades. The result was classed as good when effort intolerance changed by two grades, and fair when it changed by one grade. These results are more or less similar to those reported by other clinics (e.g. Janton, Glover and O'Neill, 1952; Sellors, Bedford and Somerville, 1953; Ellis and Harken, 1955).

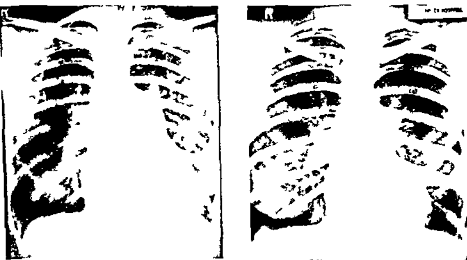


Fig. 10.2—Skiagrams (a) before and (b) two years after mitral valvotomy in a case of mitral stenosis with an extreme pulmonary vascular resistance. In (b) there is considerable reduction in the size of the right ventricle, the pulmonary artery is less dilated and there is a gap in the left border of the heart which was previously occupied by the left atrial appendix.

When the results were analysed more fully it was found that the surgical mortality in uncomplicated cases of simple mitral stenosis was only 1·7 per cent, whereas it was 33 per cent in cases with an extreme pulmonary vascular resistance, 13 per cent when aortic valvotomy was carried out as well, and 6·2 per cent when mitral stenosis was complicated by significant incompetence.

*Post operative re assessment*

It has become customary to judge the results of valvotomy by the improvement in the patients' effort tolerance and it has been stated repeatedly that the physical signs do not change much. It must be pointed

out however that following a dramatic operation of this kind patients may become psychiatrically conditioned not to recognise cardiac symptoms and *I have more than once found a patient in frank congestive failure who* alleged that he was symptom free Objective tests of effort tolerance and physiological studies of circulatory behaviour are more reliable There is no doubt also that the physical signs may change materially when a technically successful valvotomy has been performed the presystolic murmur disappears, the first heart sound becomes far less accentuated the opening snap is distinctly late and the mitral diastolic murmur shortens considerably Radiologically pulmonary venous congestion diminishes the left ventricle may fill out and in pulmonary hypertensive cases the dilated right ventricle shrinks (fig 10 22)

Post operative cardiac catheterisation in successful cases reveals a considerable fall in left atrial and pulmonary artery pressures a rise in cardiac output a fall in pulmonary vascular resistance in cases with active pulmonary hypertension and a gratifying increase of the Ry/s ratio mitral stenotic index and calculated transverse section of the mitral orifice

*Subsequent course*

In technically successful cases the marked improvement in effort tolerance has been well maintained in the majority of cases but relapse due to re stenosis has occurred at an approximate rate of 2 per cent per annum. In the absence of re stenosis hæmoptysis systemic embolism winter bronchitis angina pectoris pulmonary œdema paroxysmal cardiac dyspnœa and pulmonary embolism have not recurred and in pulmonary hypertensive cases congestive failure has proved reversible in those that survived the operation

*Patients have been encouraged to return to work and resume active* lives Subsequent pregnancies have been encouraged and have caused no trouble apart from one instance in which toxæmia caused death from acute pulmonary œdema the valve orifice at post mortem was only slightly stenosed (2 × 1 cm)

Poor or indifferent results have been due to technical failure to relieve the stricture sufficiently the production or aggravation of mitral incompetence, or the presence or development of some other factor such as a myocardial fault aortic valve disease (always more obvious after mitral valvotomy) independent bronchitis and emphysema or psychoneurosis occasionally re stenosis has occurred remarkably quickly as in the case reported by Donzelot *et al* (1953)

## OTHER FORMS OF SURGICAL TREATMENT

Relief of pulmonary venous congestion has been achieved by *anastomosing the dorsal segment branch of the right inferior pulmonary vein to the azygos vein* (Bland and Sweet 1949 D Allaines *et al* 1949) and this type of operation may still have a place in cases that for one reason or another

cannot have a mitral valvotomy e g when there is too much mitral incompetence or when valvotomy has proved technically too difficult

*Left atrial appendectomy* was suggested as a means of preventing recurrent systemic embolism (Madden 1949) and might still be considered in cases of combined stenosis and incompetence with an unusually large atrial appendage but there is little guarantee that clots will not form in the body of the left atrium, and permanent anticoagulant therapy is probably the wiser course in these difficult cases

*Ligation of the inferior vena cava* has been carried out with the dual object of relieving pulmonary venous congestion or heart failure and preventing pulmonary embolism secondary to phlebothrombosis in the legs (Cossio and Perianes 1949) Although this operation has received a good deal of support in allegedly suitable cases it is not physiological and there are better ways of achieving the objects stated

## AORTIC INCOMPETENCE

### *FREQUENCY*

Rheumatic endocarditis accounts for 67 per cent of all cases of aortic regurgitation with or without stenosis syphilis being responsible for 19 per cent atherosclerosis for 7 per cent and bacterial endocarditis for 2 per cent (Campbell 1932) Congenital bicuspid or quadricuspid valve congenital hypoplasia and dilatation of the ascending aorta dissecting aneurysm trauma, and simple severe hypertension without atherosclerosis of the valve account for the remaining 5 per cent In cases of chronic rheumatic heart disease the aortic valve is involved in 44 per cent (Cabot 1926) The present account deals primarily with the rheumatic type

A good account of the history of aortic regurgitation was given by Rolleston (1940)

### *AGE AND SEX*

About 90 per cent of cases of dominant rheumatic aortic incompetence are between 10 and 50 years of age and have had the lesion since the original rheumatic attack In Campbell's series the average age of the patients seen was 30 Males are affected twice as frequently as females

### *CLASSIFICATION*

There are five clinical types of rheumatic aortic valve disease

1 Pure aortic incompetence
2 Aortic incompetence with trivial stenosis
3 Mixed aortic incompetence and stenosis
4 Aortic stenosis with trivial incompetence
5 Pure aortic stenosis

While this appears to be obvious it is stated for clarity and is parallel

to the five varieties of mitral valve disease Types 1 and 2 are similar physiologically as are types 4 and 5 In addition any type may be complicated by any variety of mitral or tricuspid valve disease, by any degree of myocardial dysfunction and by changes in the pulmonary vascular resistance Cases may therefore be very complex We are concerned here however with dominant aortic incompetence (type 1 or 2)

## PATHOLOGY

Rheumatic inflammation of the aortic valve may cause immediate aortic incompetence Healing usually results in thickening retraction and distortion of the cusps with permanent regurgitation In addition the cusps often become adherent to one another at their bases (fusion of the commissures) so that some degree of aortic stenosis is usual Secondary calcification is common when there is stenosis

## EFFECT ON FUNCTION

The stroke volume of the left ventricle is increased by an amount which is at least equal to the quantity of blood that leaks back during diastole The fibres of the left ventricle become considerably stretched in diastole the force of the heart beat is therefore augmented according to Starling's law The initial tension is increased isometric contraction is abbreviated maximum pressure is higher than normal and is attained earlier in systole the ejection phase is shortened and the pressure then falls away steeply in late systole In other words the shape of the pressure curve is altered so that early systole is loaded and late systole unloaded (Wiggers 1935) The large quantity of blood pumped so quickly and powerfully into the relaxed arteries during early systole causes an abrupt percussion wave followed by late systolic collapse The low diastolic pressure is due partly to the aortic reflux and partly to peripheral vasodilatation, the latter encourages forward flow Both add to the collapsing quality of the pulse

The cardiac output per minute remains about normal or may be even a little raised as it is in patent ductus arteriosus and arterio venous aneurysm which have much in common with aortic incompetence Effort tolerance is usually remarkably good until the disease is well advanced Sooner or later however left ventricular failure develops often suddenly and unexpectedly The heart then becomes overloaded and the output falls below normal

Zimmerman (1950) catheterised the left ventricle via the radial artery in 10 cases of aortic incompetence when there was no clinical evidence of failure (three cases) the left ventricular diastolic pressure was normal averaging 1 3 mm Hg whereas when there was congestive heart failure (seven cases) the left ventricular diastolic pressure ranged between 15 and 39 mm Hg and averaged 25 mm Hg It is hardly necessary to point out that in the absence of mitral stenosis the left ventricular diastolic pressure is the same as the left atrial diastolic pressure and can be measured accurately by more conventional methods

Experimental aortic incompetence brought about suddenly markedly reduces the efficiency of the heart After three or four months however left ventricular hypertrophy may be sufficient to compensate for the defect and work capacity may be normal If the valve lesion is then repaired the heart may be capable of performing more work than before When two cusps are injured however full compensation is never achieved (Dieckhoff 1936)

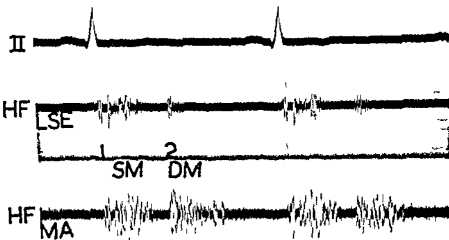



Fig 10 23—Phonocardiogram illustrating a diminuendo aortic diastolic murmur

## *CLINICAL FEATURES*

Unlike mitral stenosis, aortic incompetence develops during the stage of active valvulitis and may be at once permanent Its early diagnosis depends entirely upon recognising an aortic diastolic murmur heard best down the left border of the sternum and closely resembling the sound of a whispered *R* (*Hope* 1839) In contrast to the mitral diastolic murmur there is little or no gap between it and the second heart sound the one passing almost imperceptibly into the other Thus the usual two beat metre of the heart sounds is not altered (fig 10 23) In distinguishing aortic from mitral diastolic murmurs the greatest stress is laid on this difference in rhythm for aortic murmurs may be heard best at the apex beat It has already been explained that owing to the appreciable period that must elapse between the closure of the aortic and the opening of the mitral valves mitral diastolic murmurs give rise to a three beat dactylic cardiac metre Only when aortic incompetence is trivial is there any clinically detectable delay in the onset of the bruit for in these cases the murmur

may only be audible when there is maximum turbulence and this may not develop until the left ventricular diastolic pressure approaches zero The appearance of the murmur phonocardiographically is then diamond shaped (Wells Rappaport and Sprague 1949) As discussed under rheumatic carditis aortic diastolic murmurs of this kind may be transient in about 20 per cent of active cases

## SYMPTOMS OF ESTABLISHED AORTIC INCOMPETENCE

Effort tolerance usually remains remarkably good until the left ventricl begins to fail when breathlessness orthopnœa and paroxysmal cardiac dyspnœa develop Palpitations and throbbing however may cause dis comfort earlier Angina pectoris occurs in less than 5 per cent of cases and only when the leak is exceptionally free. Distressing attacks of pain accompanied by violent palpitations and tachycardia sometimes occur on the slightest provocation even at rest at night If the patient does not die from acute pulmonary œdema congestive heart failure sets in sooner or later sometimes it develops without clinical evidence of previous left ventricular failure as in all left sided lesions

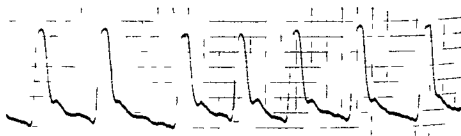


Fig 10 24—Arteriogram illustrating the water hammer pulse of aortic incompetence The percussion wave is unusually abrupt collapse precedes the pre dicrotic notch and is therefore a late systolic event

## PHYSICAL SIGNS

When incompetence is well developed numerous changes in the heart and circulation may be recognised in addition to the characteristic aortic diastolic murmur Owing to enlargement of the left ventricle the apex beat is displaced downwards and to the left and the cardiac impulse is heaving and hyperdynamic At the mitral area a diastolic murmur may develop which has all the qualities of mitral origin there is a gap between its commencement and the second heart sound, it is soft, low pitched and rumbling it may be accentuated in presystole This is the Austin Flint murmur and may depend upon interference with mitral valve function by regurgitating blood It is indistinguishable from the diastolic murmur of mitral stenosis but is rarely accompanied by a thrill

During systole the increased volume of blood flung into the circulation raises the systolic pressure and distends the aorta and large arteries The upstroke of the pulse wave is abrupt and of high amplitude (fig 10 4)

When an artery is palpated this sudden shock feels like a water hammer (a Victorian toy consisting of a small quantity of fluid in a glass vacuum tube—Watson 1843) and on auscultation the sound heard may resemble a pistol shot The pulse collapses in late systole almost as quickly as it is built up, and the diastolic blood pressure is low

The abrupt distension and quick collapse of large arteries is well seen in the carotids especially when the patient sits up This characteristic visible behaviour of an artery above heart level is Corrigan s sign (Corrigan 1832)

On auscultating the femoral or other large artery a systolic murmur is heard when the vessel is compressed when a critical pressure is applied to the artery just distal to the stethoscope a diastolic murmur may also develop The latter was first described by Duroziez (1861) whose name is attached to the sign and who attributed it to retrograde blood flow during diastole Duroziez s sign may occur however in any condition causing a large primary pulse wave a steep predicrotic notch and a conspicuous dicrotic wave Such an obstacle halts the blood flow at the pre dicrotic notch but is overcome by the dicrotic wave Above the obstacle the dicrotic wave is exaggerated below it the dicrotic wave is flattened out Hence the diastolic murmur is heard above but not below the constriction The centrifugal direction of the passage of the wave which causes the murmur has been proved by means of simultaneous multiple phonoarteriograms (Luisada 1943)

Vasodilatation exaggerates the collapsing quality of the pulse further lowers the diastolic blood pressure and causes capillary pulsation The latter may be demonstrated by lightly compressing a finger nail by transilluminating the tip of the finger or by pressing a glass slide against the lips Its presence depends upon direct transmission of the arterial pulse wave to the capillaries and it occurs in any condition in which there is sufficient relaxation of the arterioles to allow this Thus capillary pulsation may be seen in normal subjects after a hot bath in thyrotoxicosis arteriovenous aneurysm fever and in most hyperkinetic circulatory states Pulsation of the retinal veins is another common finding



Fig 10 25—Skiagram showing prominence of the aortic arch and enlargement of the left ventricle in a case of aortic incompetence

*Skiagrams* show enlargement of the left ventricle and prominence of the aorta The ascending aorta pushes the superior vena cava further to the right the aortic knob is accentuated and the descending limb appears further to the left (fig 10 25). Unfolding of the arch is seen better in the left anterior oblique position Fluoroscopy reveals exaggerated pulsation of the left ventricle and aorta When there is left ventricular failure the usual fan shaped hilar opacities of pulmonary venous congestion develop

*Electrocardiography* may provide additional evidence of left ventricular enlargement (fig 10 26)

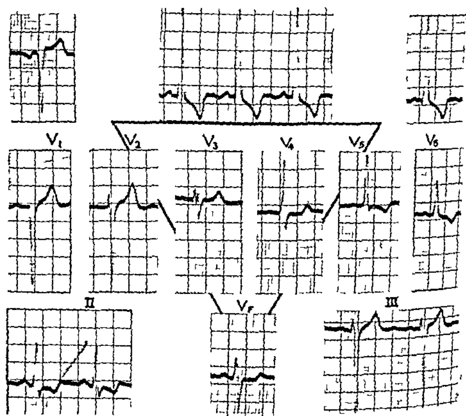



Fig 10 26—Electrocardiogram in a case of aortic incompetence showing considerable left ventricular preponderance

## DIFFERENTIAL DIAGNOSIS

Most of the features described above are common to all forms of aortic incompetence

A rheumatic etiology is favoured by a rheumatic history relatively long duration any age between 10 and 40 years signs of associated aortic stenosis with or without calcification the presence of other valve lesions absence of angina pectoris, and by a normal erythrocyte sedimentation rate

It is not always easy to be certain whether the mitral valve is stenosed when the chief lesion is obviously aortic incompetence for then a mitral pre systolic or diastolic murmur backward displacement of the œsophagus and widened bifid P waves may not have their usual significance The practical point emerges that a case presenting as one of aortic incompetence with doubtful signs of mitral stenosis is better judged rheumatic on other grounds

A *spirochætal etiology* is favoured by a history of syphilis evidence of syphilis in some other system short duration age between 40 and 60 angina pectoris absence of aortic stenosis and other valve lesions calcification of the ascending aorta but not of the aortic valve irregularities in calibre of the aortic arch or frank aneurysm an accelerated erythrocyte sedimentation rate and positive Wasserman and Kahn reactions

*Atherosclerosis* is more likely in elderly men although some of these cases are probably rheumatic primarily Angina pectoris and some degree of calcific aortic stenosis are common in this group Aortic calcification is confined to the knuckle and valve the ascending aorta being spared The erythrocyte sedimentation rate is normal and the Wasserman reaction of course negative

*Severe hypertension* presents no difficulty because the aortic leak is usually trivial and does not alter the physiology of the circulation

*Bacterial endocarditis* should be recognised by the rapid downhill course changing murmurs and liability to perforation in addition to the fever anæmia petechiæ clubbing embolism, splenomegaly hæmaturia Osler s nodes and positive blood culture

*Congenital aortic incompetence* due to *anomalous cusps* alone may be suggested by the age of the patient absence of rheumatic history and the presence of some other congenital lesion *Congenital hypoplasia of the ascending aorta* with aortic ring dilatation may be part of Marfan s syndrome (arachnodactyly) The leak in these cases may be gross Congenital aortic incompetence associated with *coarctation of the aorta or ventricular septal defect* should be obvious enough

*Dissecting aneurysm* with survival may result in severe aortic incompetence many of these cases have been mistaken for syphilis in view of the age of the patient short duration free leak absence of rheumatic history absence of stenosis and perhaps fusiform dilatation of the ascending aorta

## COURSE AND PROGNOSIS

The average life expectancy of rheumatic aortic incompetence is 20 to 30 years from its development Progno is should be based on the size of the left ventricle and upon the degree of incompetence as judged by peripheral vascular behaviour Effort tolerance often remains remarkably good until near the end Failure is commonly with normal rhythm and is usually left ventricular at first Complications are practically limited to bacterial endocarditis

*TREATMENT*

Medical care is a matter of guiding the patient in his choice of occupation limiting physical activities wisely but not unnecessarily steering a woman through or away from pregnancy, protecting the patient from bacterial endocarditis by the judicious use of prophylactic penicillin and treating heart failure by means of all the usual remedies when it arises Although trinitrin might be expected to aggravate rather than relieve angina pectoris in fact it proves beneficial more often than not, presumably by having a relatively selective action on the coronary circulation

Patients with aortic incompetence should be rejected for National Service and are usually rejected for insurance

*Surgical treatment* has so far proved unsatisfactory although Hufnagel (1954) has devised a polythene ball valve which he inserts in the descending aorta below the left subclavian artery This is said to prevent about 75 per cent of the regurgitant flow Of the first 23 cases so treated there were 17 survivors all said to be greatly improved The valve makes a considerable noise especially during the first few weeks but patients usually become accustomed to it Several cases have developed serious embolism in the legs following this operation and a small number of post operative physiological studies have revealed little if any improvement in left ventricular diastolic pressure or cardiac output The attempt to relieve aortic incompetence by surgical means however must be encouraged and better means of correcting this simple mechanical fault will no doubt be devised in due course

## AORTIC STENOSIS

*FREQUENCY*

Aortic stenosis may be congenital rheumatic or possibly purely sclerotic The frequency of rheumatic aortic stenosis partly depends on whether cases of calcific aortic stenosis in elderly subjects without a history of rheumatic fever are regarded as rheumatic or sclerotic This point has been debated for at least half a century ever since Monckeberg (1904) recognised histologically both an inflammatory and a purely sclerotic form of stricture Both macroscopic and microscopic differences between the two have been demonstrated since by many workers e g Sohval and Gross (1936) but it is by no means easy to be sure of the initial etiology when confronted by a grossly distorted and heavily calcified valve and the alleged differences are none too convincing Two painstaking pathological studies each of 200 cases of calcific aortic stenosis were those by Clawson Noble and Lufkin (1938) and Karsner and Koletsky (1947) both teams concluded that all cases were probably rheumatic Assuming this to be so rheumatic aortic stenosis is common and must occur in at least one quarter of all cases of chronic rheumatic heart disease

*PATHOLOGY*

Fibrous scar tissue representing healed aortic valvulitis usually causes fusion of the cusps at their commissures Slight narrowing at the aortic aperture is thus found in most cases of rheumatic aortic valve disease When fusion extends further up the margins of the cusps true stenosis results Valve leaflets become thick rigid distorted and often unrecognisable Secondary valve calcification is common (The aorta and large arteries often remain remarkably free from atheroma (Clawson *et al* 1938) and both the frequency and severity of coronary atherosclerosis are inversely proportional to the degree of stenosis (Dry and Willius 1939) The left ventricle hypertrophies and may finally become enormous, in a case reported by Lowe and Bate (1948) the heart weighed 2 340 G

*EFFECT ON FUNCTION*

The aortic orifice must be reduced to about one quarter of its natural size before changes in the circulation can be demonstrated (Wiggers 1935) Left ventricular pressure curves then show a rai ed initial tension steep isometric pressure gradient and an elevated maximum pressure that is reached relatively early in systole but there is no collapse as in aortic incompetence Pressure curves obtained from the aorta show an initial relatively steep rise interrupted by an anacrotic notch and followed by a slower rise that reache its maximum late in systole the maximum pressure attained is less than normal (fig 10 27) The more severe the stenosis the earlier the anacrotic notch The ejection phase is prolonged

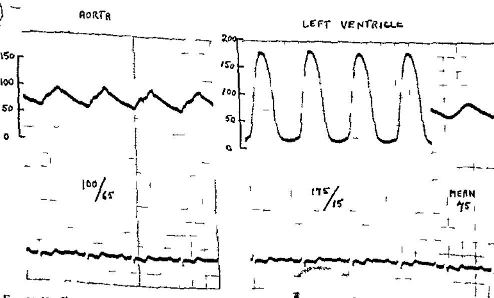



Fig 10 27—Pressure pul es from the orta and left ventricle ... pr sur grad nt of 75 mm Hg Note the ana rotic notch ... st nosis showing a systol... ummit in the aortic pul...

The systolic pressure gradient between left ventricle and aorta may be anything between a few mm Hg and over 150 mm Hg according to the severity of the stricture and the integrity of the left ventricular myocardium With a gradient of only 5 mm Hg in mild cases or in cases of mixed stenosis and incompetence the aortic pulse may still show an anacrotic notch and slow secondary rise (fig 10 28)

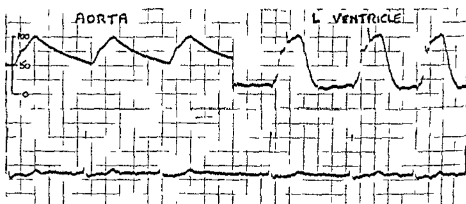



Fig 10 28—Pressure pulses from the aorta and left ventricle in a case of aortic stenosis and incompetence The pressure gradient is less than 5 mm Hg but the aortic pulse is stenotic in form

To maintain the stroke volume and cardiac output great power must be developed by the left ventricle The chamber is more hypertrophied and less dilated than in aortic incompetence Its increased initial tension is partly due to more forceful left atrial systole the left ventricle is deprived of this important help in cases of coincident mitral stenosis

The cardiac output per minute is strictly limited as in mitral pulmonary and tricuspid stenosis and in severe cases is reduced at rest The low mean aortic pressure prevents the coronary blood flow from keeping pace with the increased demands of the left ventricle

## *CLINICAL FEATURES*

### *Sex and Age*

Aortic stenosis is at least twice as common in men as in women The lesion may be discovered at any time from adolescence to old age usually in the sixth decade Female patients tend to be younger than male

### *Symptoms*

Patients with aortic stenosis may complain of syncope (10–20 per cent) angina pectoris (20–36 per cent) or symptoms referable to left ventricular or congestive heart failure (Contratto and Levine 1937 Mitchell *et al* 1954)

*Syncope* is of two kinds cardiac and vasomotor Cardiac syncope is abrupt and fleeting and when it occurs on effort may be due to acute left ventricular failure or to a fixed low cardiac output so that the blood pressure cannot be maintained when peripheral vasodilatation occurs Cardiac syncope at rest may be due to paroxysmal ventricular fibrillation or possibly to locking of the valve (de Veer 1938) Such attacks herald sudden death from a similar mechanism The low blood pressure of aortic stenosis predisposes to vasomotor and orthostatic syncope

*Angina pectoris* depends upon poor coronary filling due to the low mean blood pressure and low fixed cardiac output on effort the heavy demands of the hypertrophied and overworking left ventricle have little chance of being adequately met The pain is indistinguishable in site quality duration and behaviour to that associated with occlusive coronary atherosclerosis and may finally occur on the slightest effort or even at rest as in advanced coronary disease

*Breathlessness* on effort is of course the commonest symptom and sooner or later orthopnœa paroxysmal cardiac dyspnœa or acute pulmonary œdema may occur as a result of left ventricular failure Œdema due to congestive heart failure may occur later or may develop without previous evidence of left sided failure as in hypertensive heart disease

*The physical signs* are as follows

1 There is sometimes a delicate pale pink complexion – the Dresden china look

2 The pulse is characteristic when relatively slow (fig 10 29) being small and sustained (plateau or slow rising pulse) It depends upon the longer duration of left ventricular systole the low blood pressure and upon the delayed development of maximum aortic pressure These features tend

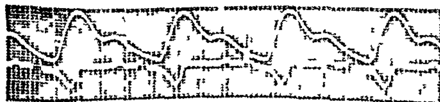


Fig 10 29—Arteriogram in a case of aortic stenosis The percussion wave is prolonged and the maximum pressure is reached late in systole The phonocardiogram above shows a typical mid systolic murmur

(By courtesy of Dr Evan Gardner and Max Zoob)

to disappear as the heart rate quickens The anacrotic notch of the aortic tracing may or may not be felt at the periphery for it tends to be ironed out by the elasticity of the arteries (fig 10 30) When aortic incompetence is present as well the pulse assumes a bisferiens quality (fig 10 31) To the palpating finger it feels double and may even be mistaken for coupling

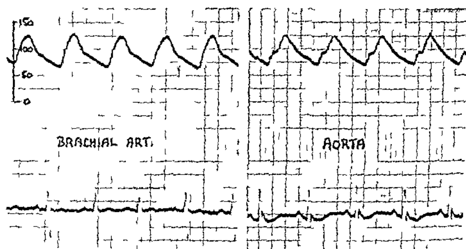



Fig 10 30—Pressure pulse from the brachial artery and aorta in a case of aortic stenosis showing disappearance of the anacrotic notch in the more peripheral tracing

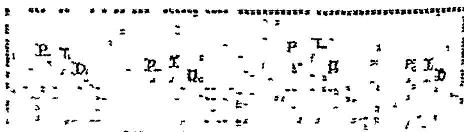


Fig 10 31—Arteriogram illustrating pulsus bisferiens in a case of combined aortic stenosis and incompetence I is the percussion wave T the tidal wave both are systolic events (B[illegible] (D[illegible] F[illegible] Gard[illegible] [illegible] Zoob)

*due to premature ectopic beats* Both waves occur during the ejection phase According to Bramwell (1937) the second impulse is tidal in nature being due to overlapping and partial fusion between a forcible but prolonged percussion wave and its reflection from the periphery Aortic incompetence increases the force of the percussion wave aortic stenosis prolongs it Neither alone will produce this pulse Direct intra arterial pressure tracings show a plateau rather than a dip following the percussion wave and preceding the tidal wave (fig 10 32) The discrepancy may be due to the fact that both the palpating finger and any type of tambour used for




10 32—D rect arteriogram from a case of aortic stenosis and incompetence sho ing au instead of a dip between percu sion and tidal wa es Clinically this was a classical pulsus b sferiens

ding arterial pulsation from without must apply suitable pressure on rtery usually approximating the diastolic pressure both finger and our move through distances proportional to the pulse pressure so they record the sudden halting of the percussion wave as a negative ure for they have upward momentum at the time

The blood pressure is variable In severe cases it is low and the pulse ure small but in mild or moderate cases or when there is recognisable aortic incompetence it may be elevated and the pulse pressure may be increased About 10 per cent are truly hypertensive—an incidence a good deal lower than in controls of the same age group

4 The apex beat is displaced downwards and to the left and the cardiac impulse is quietly heaving The left ventricle is hypertrophied rather than dilated

5 A basal systolic thrill is usually present It is best appreciated when the patient leans forward and stops breathing in full expiration It may be most intense either to the right or left of the sternum A systolic thrill may also be felt over the carotid or subclavian arteries Although such a thrill is not diagnostic of aortic stenosis it is suggestive and encourages prolonged search at the base

6 A rough basal systolic murmur is almost invariable It is conducted into the cervical arteries and may be heard remarkably well at the apex beat over the left ventricle The murmur is mid systolic (fig 10 29) starting when the aortic valve opens at the end of the period of isometric contraction and finishing in physiological protodiastole when the left ventricle begins to relax appreciably before the aortic second sound (Leatham 1951) When best heard at the apex beat its timing at once distinguishes it from the pan systolic murmur of mitral incompetence When best heard at the base an aortic systolic murmur may be distinguished from a pulmonary murmur not only by its shorter duration but

also by its delayed return after the Valsalva manœuvre (Zinsser and Kay, 1950))

7 An aortic systolic ejection click immediately precedes the murmur in many cases (Lian and Welti 1937) When heard at the apex beat this click may be mistaken for the first heart sound, and the real first heart sound for presystolic left atrial gallop the murmur is then erroneously believed to be early systolic and a diagnosis of incipient left ventricular failure with functional mitral incompetence may be wrongly made

8 The aortic component of the second heart sound is characteristically delayed in the majority of cases and absent in a minority the delay is attributed to prolongation of left ventricular systole and to the time occupied by the relaxing left ventricle in abolishing the systolic pressure gradient across the valve an absent aortic second sound is due to almost complete immobilisation of a heavily calcified rigid valve These changes result in a single second heart sound the aortic element being synchronous with the pulmonary or absent altogether or in reversed splitting of the second heart sound the aortic component falling after the pulmonary so that the split widens during expiration instead of during inspiration (Leatham 1952)) When the second heart sound is single the two components are probably fused if the sound can be heard at the apex beat and over the right carotid artery if the single second sound can be heard only at the pulmonary area the aortic component is probably absent



Fig 10 33—Skiagram of a case of aortic stenosis showing great enlargement of the left ventricle slight prominence of the ascending aorta and hilar congestion

9 On fluoroscopy the left ventricle looks dense and bulky The aorta may be conspicuous or relatively hypoplastic (fig 10 33) Post stenotic dilatation of the ascending aorta is usually more obvious at operation than in skiagrams because the shadow of the aortic root tends to merge with that of the ventricles and right atrium When the lower part of the ascending aorta is conspicuous however and the rest of it inconspicuous the presence of aortic stenosis is strongly confirmed Calcification of the aortic valve can be seen in most cases particularly if the patient is over 50

10 The electrocardiogram usually provides convincing

evidence of left ventricular enlargement Perhaps owing to the concentric type of hypertrophy and to the lack of dilatation the heart is often electrically vertical Standard leads then show the concordant pattern of left ventricular preponderance (fig 10 34) Exceptionally high voltage R waves are characteristic of aortic stenosis T is frequently inverted in leads facing the surface of the left ventricle Left bundle branch block varying degrees of atrioventricular block and atrial fibrillation each occur in about 10 per cent of cases (Mitchell *et al* 1954)

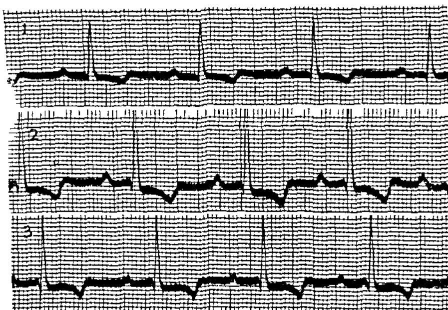



FIG 10 34—Electrocardiogram in a case of aortic stenosis showing concordant left ventricular preponderance in standard leads the heart being vertical

## *SPECIAL TESTS*

*Indirect or direct arteriograms* of the brachial pressure pulse confirm the anacrotic or bisferiens pulse that is felt In doubtful cases these tracings may be helpful A normal brachial pressure pulse occupies about 0 16 seconds from its onset to the beginning of the sharp downstroke the initial upstroke or front of the percussion wave measuring 0 08 second and the blunt peak also 0 08 second In aortic stenosis the front of the percussion wave occupies 0 08 to 0 12 second to the anacrotic notch (fig 10 32) or to the beginning of the blunt peak if the notch is ironed out (fig 10 30), and the blunt peak itself occupies about 0 12 second so that from its onset to the beginning of the sharp downstroke the pulse occupies at least 0 20 second and usually 0 24 second

If the pulsus bisferiens dominant aortic stenosis is favoured if the tidal wave is taller than the percussion wave dominant aortic incompetence if it is the other way about (fig 10 32)

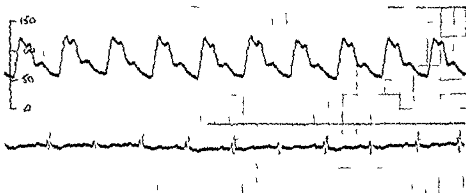



Fig 10 35—Direct arterial tracing illustrating the pulsus bisferiens in a case of aortic stenosis and incompetence with a dominant leak the percussion wave is taller than the tidal wave

*Cardiac catheterisation* may be helpful in assessing the degree of coincident mitral stenosis measuring the force of left atrial systole determining the left ventricular diastolic pressure and estimating the cardiac output at rest and on effort

Neither a powerful *a* wave in the indirect left atrial pressure pulse nor the level of the mean left atrial pressure provides any evidence of mitral *valve disease in* cases of severe aortic stenosis for the former may be a manifestation of left ventricular stress and the latter the result of left ventricular failure (fig 10 36) If the *left atrial pressure* is raised only the Ry/v ratio indicates whether the mitral valve is obstructed or not In figure 10 36 Ry/v measures at least 5 so that the high left atrial pressure is obviously due to left ventricular failure or gross mitral incompetence In figure 10 37 on the other hand Ry/v is 1 3 and the raised left atrial pressure is due to coincident mitral stenosis

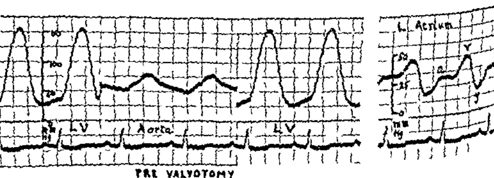
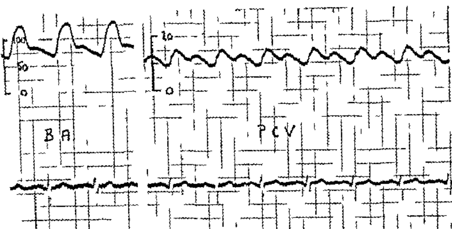



Fig 10 36—Pressure pulses from the aorta left ventricle and left atrium in a case of aortic stenosis with left ventricular failure Note the very rapid *y descent* and conspicuous *y* trough in the left atrial tracing The Ry/v ratio is 5




g 10 37—Typical wedged pulmonary artery tracing (P C V ) from a case of combined mi and mitral stenosis showing an Ry v ratio of 1 3 in the indirect left atrial pressure pulse

*Giant a waves* in the left atrial pressure pulse have been described by orlin (1955) and are believed to be the counterpart of giant *a* waves in ne right atrium in cases of severe pulmonary stenosis Extra care may be necessary at times however to make sure that what is taken for *a* at first sight is not in fact *c* for accurate interpretation of wedged pulmonary artery tracings is not always easy

The *left ventricular diastolic pressure* can only be measured from direct or indirect left atrial pressure tracings when mitral stenosis can be excluded i e when the Ry/v ratio is over 1 6 A good example from a case with left ventricular failure is shown in figure 10 36 in which direct pressure tracings have been recorded from both left atrium and ventricle The raised left ventricular diastolic pressure can of course be inferred from the patient s symptoms and from the radiological appearances of the lungs

*Estimation of the cardiac output* at rest and on effort may be important when the severity of a case of aortic stenosis is in doubt It also provides essential data for interpreting the significance of any given pressure gradient across the aortic valve *Dye concentration curves* may be recorded with this object when the pressure gradient is being measured at operation Good outputs at rest and on effort are maintained in cases of aortic stenosis until relatively late in their course (Goldberg Bakst and Bailey 1954)

*The pressure gradient across the aortic valve* may be measured by recording simultaneously or in immediate succession both *left ventricular and* brachial pressure pulses (fig 10 36) The former may be achieved by threading a fine polythene catheter through a needle inserted directly into the left atrium from behind and manipulating it until its tip passes through the mitral valve (Bjork *et al* 1954 1955) Alternatively a needle may be passed directly into the left ventricle from the region of the apex

beat At Brompton the latter has proved safe and far less traumatic but should be undertaken only by skilled surgeons who must be prepared to carry out an immediate aortic valvotomy should ventricular fibrillation occur If the information is to be of any real value, forward flow should be measured at the same time, and if there is appreciable aortic incompetence this is impossible at the moment

*Phonocardiography* is of real value when the nature of the systolic murmur is in doubt when there is clinical difficulty in distinguishing left atrial gallop at the apex beat from an aortic ejection click and when the timing of aortic valve closure cannot be ascertained clinically

The *ballistocardiogram* in aortic stenosis has been studied by Van Lingen *et al* (1952) A characteristic angulated or outwardly bowed J K segment was described in tracings obtained from a low frequency critically damped instrument

*Tomography* is a good method of recording calcified aortic valves (Davies and Steiner 1949)

## *COMPLICATIONS*

If syncope angina pectoris changes of rhythm left ventricular failure, congestive heart failure and heavy calcification are all regarded as manifestations of the disease itself as they should be then the only complication of rheumatic aortic stenosis is bacterial endocarditis which sooner or later occurs in about 10 per cent of cases In the large series reported by Mitchell *et al* (1954) bacterial endocarditis accounted for 20 per cent of the deaths

## *DIFFERENTIAL DIAGNOSIS*

If as much attention were paid to the quality of the peripheral pulse as to cardiac murmurs serious aortic stenosis would be both less frequently overlooked and less often diagnosed in error nevertheless the pulse is normal in mild cases The chief sources of confusion include functional basal murmurs mitral incompetence ventricular septal defect coarctation of the aorta and a group of normotensive low output cardiopathies that may involve mainly the left ventricle such as acquired subendocardial fibrosis

*Innocent basal ejection murmurs* are mid systolic especially when aortic When associated with a high cardiac output as in anæmia they present little difficulty in diagnosis but when occurring alone in young persons or in association with atherosclerosis of the aorta in the elderly slight aortic stenosis is difficult to exclude A number of cases of advanced calcific aortic stenosis that have been seen in the last few years were diagnosed as having a functional systolic murmur during the first world war A similar number of young people who have this murmur at the present time are therefore being watched with considerable interest although strongly encouraged to lead normal lives

*Mitral incompetence* should be distinguished by the sharper quality of the pulse the hyperdynamic nature of left ventricular pulsation the

pan systolic timing of the thrill and murmur the small ascending aorta and the enlarged left atrium. As previously stated the murmur of aortic stenosis may be maximum at the apex beat over the surface of the left ventricle. When valve calcification is recognised the position of the opacity should determine whether it is aortic or mitral

*Ventricular septal defect* should also be distinguished by the hyper dynamic quality of ventricular pulsation and the pan systolic timing of the bruit and thrill in addition characteristic changes *in the electrocardiogram* and skiagram help to prevent error In doubtful cases cardiac catheterisa *tion should demonstrate the shunt*

*Certain cardiopathies* usually of unknown etiology may present with clinical electrocardiographic and radiological evidence of predominant left ventricular enlargement a low or normal blood pressure small rapid pulse and a low cardiac output (If there is a murmur it is usually apical and pan systolic being caused by functional mitral incompetence) The absence of demonstrable valve calcification may be attributed to the size and density of the heart so that the observer does not feel confident of his negative findings Cases of this sort can be awkward and diagnostic mistakes have been made in both directions (One of the sources of confusion is the belief that in about 10 per cent of cases of aortic stenosis no *rtic systolic murmur can be heard at any time as reported by Bergeron et al* (1952)) A more convincing statement would be that no *mid systolic murmur* could be heard at any time at base *or apex* by an experienced cardiologist such a statement has yet to be made In doubtful cases a phonocardiogram and intra arterial pressure tracing should be recorded and every effort made to reveal valve calcification If the diagnosis is still uncertain the pressure gradient across the aortic valve should be measured for aortic stenosis must not be missed

In *combined aortic stenosis and incompetence* the difficulty is to decide which is dominant This is essential when selecting cases for aortic valvotomy Since the operation was introduced it has been discovered that *physiologically in mixed cases there is often more incompetence* and less stenosis than traditional evidence would lead one to suppose rarely vice versa For example an obvious pulsus bisferiens seems to indicate domi nant incompetence rather than stenosis neither angina pectoris a diastolic pressure of 80 mm Hg a coarse aortic systolic thrill nor heavy valve calcification has proved reliable evidence of dominant stenosis The mixed case in fact is causing great confusion and even measuring the pressure gradient across the valve is useless without knowing the forward flow At present if a case has more than trivial aortic incompetence so that a *problem does in fact arise* the probability is that the leak is too great to warrant valvotomy and until more is known this may be the best attitude to adopt We have *recorded pressure gradients up to 100 mm* Hg across the aortic valve in cases of dominant incompetence subsequently proved at operation

*Combined aortic valve disease and mitral stenosis* usually presents less difficulty because the degree of mitral stricture can be worked out with precision and if this demands valvotomy then the pressure gradient across the aortic valve can be measured at operation easily enough If the mitral stenosis is relatively unimportant the problem reverts to that just discussed It may be noted here however that well developed mitral valve disease damps all the signs of aortic valve disease and these may become much more evident following mitral valvotomy

*Etiological diagnosis* may also be difficult Rheumatic aortic stenosis must be distinguished from congenital and calcific atherosclerotic varieties Congenital stenosis may be clinically indistinguishable from the rheumatic variety but the lesion is usually discovered in childhood there is no rheumatic history and incompetence is unusual

It is uncertain whether calcific aortic stenosis in elderly or middle aged subjects is atherosclerotic or rheumatic Thus eleven of twenty one cases reported by Christian (1931) gave a history of rheumatic fever Dry and Willius (1939) obtained a rheumatic history in 22 per cent of 228 cases and Clawson Noble and Lufkin (1938) found a rheumatic history in 35 per cent of 200 cases On the other hand in the quoted series of Dry and Willius there were 91 necropsied cases without disease of other valves a rheumatic history was obtained in only four of these—the usual incidence in any series of normal controls Again in the quoted series of Clawson and his colleagues 20 5 per cent of the patients were under 41 years of age and 39 per cent were under 51 moreover 89 had a mitral lesion as well It is obvious that many of these cases were rheumatic but this has little bearing upon the question of whether or not pure calcific aortic stenosis in elderly people is rheumatic On the pathological side Clawson (1931) particularly has drawn attention to the frequency of inflammatory stigmata of the rheumatic type but others notably Sohval and Gross (1936) have been unable to confirm such findings The best evidence of a rheumatic or other inflammatory etiology is perhaps the remarkable absence of atherosclerosis in the aorta and coronary arteries in most cases All observers have agreed on this point that these vessels must have been long protected by the stenosis However Monckeberg s original thesis that calcific aortic stenosis in elderly subjects may be degenerative (Monckeberg 1904) has not been altogether disproved

Clinically calcific aortic stenosis in elderly subjects behaves like rheumatic aortic stenosis

## COURSE AND PROGNOSIS

As already mentioned the initial rheumatic attack in cases of more or less pure aortic stenosis is sub clinical in about 80 per cent of cases A mid systolic murmur however is often heard when the patient is young and well whether maximum at apex or base this murmur has usually been regarded erroneously as functional Sooner or later according to the

everity of the lesion attacks of syncope (15 per cent) or angina pectoris (33 per cent) may develop Both are serious and limit future life expectancy to an average of 3 3 and 4 1 years respectively (Mitchell *et al* 1954) Abrupt death without immediate warning presumably from ventricular fibrillation or cardiac standstill occurs in 18 per cent of severe cases Horan and Barnes 1948 Mitchell *et al* 1954) and is by no means confined to those who have had syncope or angina pectoris Subacute bacterial endocarditis may develop any time in 10 per cent of cases and accounts for 20 per cent of the deaths (Contratto and Levine 1937 Mitchell *et al* 1954) The majority of patients who survive these hazards succumb to left ventricular or congestive heart failure before reaching the age of 70 Heart failure accounted for 30 to 50 per cent of the deaths in the various series quoted above and its onset usually limits further life expectancy to 2 years

The total mortality from aortic stenosis increases in a linear manner from the third to the seventh decade (Dry and Willius 1939) after which it falls again but there are as many deaths in the eighth decade as in the sixth No distinction is made here between rheumatic and calcific aortic stenosis The average age at death is 55 to 65 women tending to be a decade younger than men

In any given case the *prognosis* varies between excellent in those with no more than an aortic systolic murmur and a life expectancy of only 2 3 or 4 years from the onset of heart failure syncope or angina pectoris respectively Between these two extremes the prognosis in symptom free cases of unmistakable aortic stenosis may be assessed by recognising three grades of severity based on the physical signs electrocardiogram and skiagram Mild cases with only slight hypertrophy of the left ventricle an aortic systolic thrill and murmur aortic ejection click and closely split or single second heart sound may be expected to remain symptom free for at least 20 to 30 years cases of moderate severity with alteration of the peripheral pulse hypertrophy of the left ventricle moderately delayed aortic valve closure grade 1 to 2 left ventricular preponderance electrocardiographically and slight enlargement of the left ventricle radiologically may be expected to live 10 to 20 years severe cases, as yet symptom free having the fully developed physical signs electrocardiogram and fluoroscopic appearances described above—particularly an unmistakable anacrotic pulse heaving left ventricle reversed splitting of the second heart sound inverted T waves in left ventricular surface leads or their equivalents and obvious enlargement of the left ventricle radiologically—cannot be expected to survive more than 5 to 10 years

## TREATMENT

*Medical management* is similar to that of aortic incompetence Little can be done to prevent syncope other than restricting physical effort For

angina pectoris trinitrin is again of benefit more often than not, despite its theoretical objections

*Aortic valvotomy* (Bailey *et al* 1952) has proved more difficult and less satisfactory than mitral valvotomy The approach is through the anterior wall of the left ventricle Bailey uses a tri fin expanding dilator on a swivel head which is said to adjust itself to the commissures (Larzelere and Bailey 1953) although cinematographic demonstration of aortic valve function in cases of advanced aortic stenosis reveal so much fusion and distortion of the cusps that three commissures can rarely be made out (McMillan 1955) Simple two bladed expanding dilators may be just as effective (or ineffective)

The present high mortality of 22 per cent from aortic valvotomy (Bailey *et al* 1954) is partly due to the very advanced type of case surgeons have been invited to tackle usually those with severe angina pectoris or heart failure The physician s difficult obligation is to advise the operation in severe cases before these manifestations of impending disaster arise i e when the patient *is still virtually symptom free* and that *is no easy matter for the risk is still appreciable and the physiological result rarely excellent*

As previously stated a common mistake is to under estimate the degree of aortic incompetence present this should not be more than trivial clinically if dominant stenosis is to be confirmed surgically The error has always *been in the same direction i e subsequent necropsies in cases rejected for valvotomy on the grounds of too much aortic incompetence* have yet to show dominant stenosis It is repeated here for emphasis that neither angina pectoris syncope pulsus bisferiens a diastolic blood pressure of 80 to 85 mm Hg nor valve calcification can be *accepted as evidence of dominant stenosis in these mixed cases even a systolic pressure* gradient of 50 to 100 mm Hg across the aortic valve is inconclusive unless the forward stroke flow is known In classical cases of more or less pure severe stenosis the gradient is usually 50 to 150 mm Hg but is greatly influenced by the cardiac output at the time

So far at *Brompton*, 50 cases have been operated on mostly by Sir Russell Brock with a mortality of 22 per cent All these cases were advanced many far too advanced It is too early to assess the post operative results in the survivors with any precision, but it is fair to say that the *best tend to be good rather than excellent* and that the majority are fair rather than good In a technically successful case a ventricular aortic pressure gradient of 50 to 100 mm Hg should be reduced to below 20 mm Hg (fig 10 38) Results of this kind are more likely to be achieved if aortic valvotomy is carried out earlier

*Combined aortic and mitral valvotomy* has proved very encouraging (Likoff *et al*, 1955) It is probable that in these cases symptoms due to mitral stenosis have forced operative treatment at a time when the aortic lesion itself might have caused no symptoms at all in other words some of these cases are giving surgeons an opportunity *to relieve* aortic stenosis

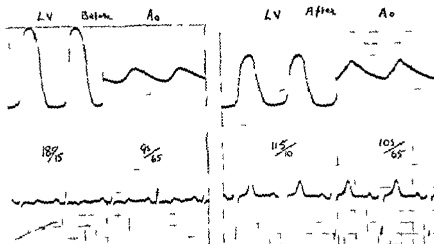



Fig. 38.—Pressure pulses from the left ventricle and aorta in a case of aortic stenosis before and after aortic valvotomy the pressure gradient across the aortic valve has been reduced from 90 to 10 mm Hg

when it is not too far advanced Technically most surgeons have so far preferred to undertake mitral valvotomy first, being the less hazardous of the two for ventricular fibrillation or standstill occurring during aortic valvotomy might be very difficult to correct in the presence of unrelieved mitral stenosis )

## TRICUSPID INCOMPETENCE

Tricuspid incompetence may be functional or organic the former being secondary to right ventricular dilatation with expansion of the tricuspid ring as may occur in cases of pulmonary hypertension pulmonary stenosis with normal aortic root atrial or ventricular septal defect or right ventricular failure from any cause When there is pulmonary hypertension secondary to *mitral stenosis* clinical distinction between functional and organic tricuspid incompetence may be difficult in the first instance but the course and response to digitalis and rest may clarify the issue functional incompetence may be temporary, organic tricuspid disease is always permanent

The majority of cases of chronic rheumatic tricuspid valve disease have some degree of stenosis and the majority of cases of frank tricuspid incompetence are functional Rheumatic tricuspid disease will therefore be discussed as a whole under tricuspid stenosis and the following remarks apply chiefly to functional tricuspid incompetence

### *FREQUENCY*

At the present time it may be unwise to attempt to assess the frequency of functional tricuspid incompetence because accurate criteria upon which

its diagnosis may be based with confidence have yet to be set up In my own cases considerable or gross tricuspid incompetence with physical signs that would be generally accepted occurred at one time or another in 22 out of 32 cases of mitral stenosis complicated by an extreme pulmonary vascular resistance (over 10 units) but in only one out of 14 cases of primary pulmonary hypertension three out of 52 cases of severe pulmonary valve stenosis with normal aortic root (R V systolic pressure over 100 mm Hg) and 10 out of 98 cases of severe atrial septal defect (pulmonary flow at least three times the systemic flow or high pulmonary vascular resistance) This curious discrepancy was found to be due to the presence or absence of atrial fibrillation Thus in the mitral group atrial fibrillation occurred in 62 per cent tricuspid incompetence was recognised in 91 per cent of these fibrillating cases and in only 10 per cent of those with normal rhythm In the other three groups atrial fibrillation occurred in only 8 2 per cent tricuspid incompetence was found in 87 per cent of these but in only one out of 149 cases with normal rhythm These rather startling figures make it only too clear that what is customarily taken for tricuspid incompetence is closely related to atrial fibrillation whatever the explanation may be

## *HÆMODYNAMICS*

The effect of tricuspid incompetence on right ventricular output and filling and on the right atrial and systemic venous pressure pulse is similar in all respects to the effect of mitral incompetence on the left side of the heart and pulmonary venous circulation Functional tricuspid incompetence occurs when the right ventricle and tricuspid ring dilate as a result of failure or a physiological situation close to failure This results in initial diminution of forward flow by the amount of blood that regurgitates during systole The larger volume of blood in the right atrium however increases the pressure of the *v* wave so that when the right ventricle relaxes it is subjected to a higher filling pressure than before and dilates further to accommodate the extra blood In this sense augmented diastolic filling compensates for the leak The increased right ventricular dilatation however may cause a greater degree of tricuspid incompetence so that a vicious circle may become established forces acting in the opposite direction are myocardial resistance to unlimited diastolic stretch and the restraining influence of the pericardium so that the situation is quickly stabilised

The right atrial pressure pulse is similar to the left atrial pressure pulse in cases of mitral incompetence and is characterised by an unusually large *v* wave followed by a rapid *y* descent and deep *y* trough (fig 10 39) The 'overshoot in the early part of the right ventricular diastolic pressure tracing slightly precedes the *y* descent there being a strong potential pressure gradient from atrium to ventricle as the pressure within the latter falls rapidly to zero These appearances are identical with those found in

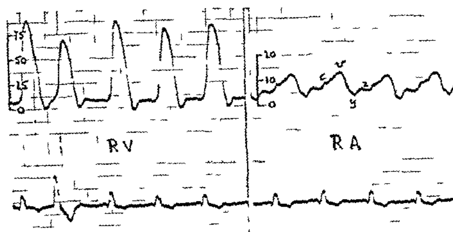



Fig 10 39—R V and R A pressure pulses from a case of severe pulmonary valve stenosis with functional tricuspid incompetence There is 2–1 atrial flutter (not well shown) and right B B B Note the absence of the x descent the steep y descent and the conspicuous y trough in the R A tracing and the so called overshoot in the R V tracing

cases of Pick s disease when the likelihood of tricuspid incompetence seems remote In the illustration shown there is 2–1 atrial flutter (not well seen in the electrocardiographic lead recorded) and right bundle branch block The *x* descent is absent as in most cases of atrial fibrillation (or flutter) just as it is in left atrial pressure tracings in cases of atrial fibrillation even when it is known for certain that there is no mitral incompetence Since nearly all cases of functional tricuspid incompetence that are recognised as such have atrial fibrillation disappearance of the *x* descent does *not* provide convincing evidence of the diagnosis despite traditional belief to the contrary Certainly the magnitude of *v* can be so great in florid cases of tricuspid incompetence as to be hard to reconcile with any other diagnosis but that is another matter Certainly all cases of tricuspid incompetence with normal rhythm and with jugular pulses having two crests and two troughs (*a* *x* *v* and *y*) are being overlooked For current expressions of the other view based on careful physiological studies the reader is referred to papers by Bloomfield *et al* (1946) Muller and Shillingford (1954) and Korner and Shillingford (1954)

## CLINICAL FEATURES

*Age* and *sex* are related to the underlying disease not to the tricuspid incompetence

The only *symptoms* that are directly attributable to the leak are venous throbbing in the neck and abdomen swelling of the abdomen from gross enlargement of the liver and perhaps ascites and œdema although these are partly due to the primary disease tricuspid incompetence however

diminishes the cardiac output further In very advanced cases there may be impairment of hepatic function and hepatic psychosis

The *physical signs* include an unusually large v wave in the jugular pulse followed by a rapid y descent and conspicuous y trough (fig 10 40)

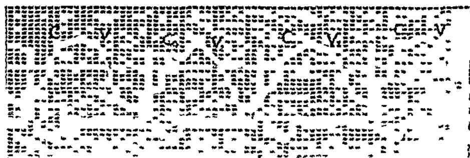



Fig 10 40—Jugular phlebogram showing fusion of the c and v waves in a case of tricuspid incompetence owing to atrial fibrillation the a wave is absent
(By ... f D M x Zoob)

systolic pulsation of the liver synchronous with the large v wave, occasionally systolic pulsation of peripheral veins also (when the venous valves have become incompetent) a hyperdynamic right ventricular thrust a pansystolic murmur (with or without a thrill) that waxes during inspiration and which may be heard anywhere over the distended right ventricle from the left sternal edge to the apex beat (usually formed by the right ventricle in these cases) and sometimes a short functional tricuspid diastolic murmur as well

The great majority of recognised cases are associated with atrial fibrillation as previously pointed out and either because of this or because

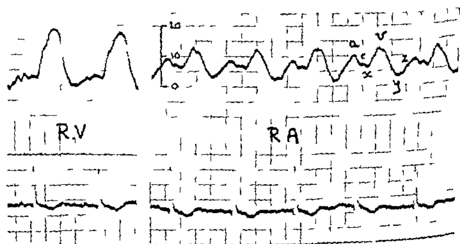



Fig 10 41—Right ventricular and right atrial pressure pulses from a case of organic tricuspid incompetence with normal rhythm showing preservation of the v descent and a conspicuous y trough



Fig 10 42—Skiagram showing gross dilatation of the right atrium with a blunt right cardio phrenic angle in a case of tricuspid incompetence

### *TREATMENT*

Bed rest and full treatment for heart failure is advisable in the first instance to see whether the tricuspid incompetence is reversible If not the patient should be allowed up and about, although treatment for heart failure should be continued

## TRICUSPID STENOSIS

Although organic disease of the tricuspid valve is found at necropsy in 10 to 20 per cent of all cases of chronic rheumatic heart disease (Cooke and White 1941 Smith and Levine 1942) clinical tricuspid stenosis is infrequently recognised It is nearly always accompanied by mitral stenosis (Pitt 1909) often by aortic valve disease as well In my own analysed series of some 500 cases of rheumatic heart disease tricuspid stenosis was found in 4 per cent, since the majority of these 500 cases were catheterised and the tracings inspected carefully for the tell tale pressure gradient the frequency given is believed to be accurate

### *ETIOLOGY*

Tricuspid stenosis is nearly always rheumatic Both disseminated lupus and argentaffinoma however may cause it and congenital cases have been reported

### *PATHOLOGY*

The development of chronic tricuspid valve disease following active endocarditis presumably resembles the march of events in mitral disease but the end result is somewhat different in that fusion is said to result more often in a single valve curtain perforated by a central or eccentric roundish hole than in button hole stenosis Although some degree of incompetence would therefore be expected in the majority of cases physiological studies suggest that stenosis is the commoner lesion How this tallies with necropsy evidence to the contrary remains to be seen Aceves and Carral (1947) for instance found tricuspid valve disease in 33 per cent of 147 consecutive necropsies in cases of rheumatic heart disease of these 11 were stenosed 28 incompetent and 11 mixed It is possible therefore that cases of organic tricuspid incompetence are being overlooked clinically

### *HÆMODYNAMICS*

Tricuspid stenosis tends to prevent proper filling of the right ventricle and therefore both lowers the cardiac output and relieves pulmonary venous congestion caused by mitral stenosis, which is invariably present The obstruction results in elevation of the right atrial pressure and in a presystolic (fig 10 44) or diastolic pressure gradient (fig 10 45) across the tricuspid valve, similar in all respects to the pressure gradient across the mitral valve in cases of mitral stenosis (fig 10 46) The presystolic gradient

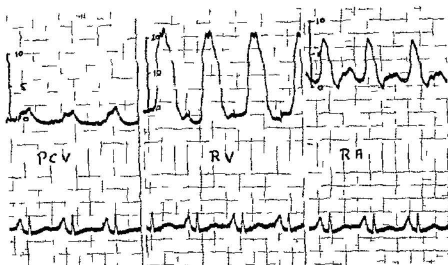



Fig 10 44—Intracardiac pressure pulses from a case of tricuspid stenosis with normal rhythm showing giant *a* waves in the right atrial tracing and a presystolic pressure gradient across the tricuspid valve

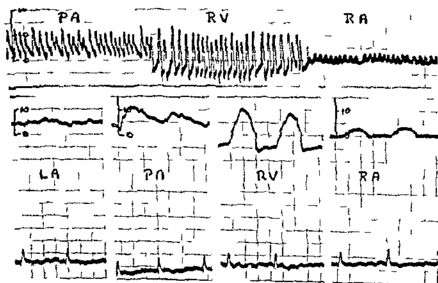



Fig 10 45—Intracardiac pressure pulses in a case of tricuspid stenosis with atrial fibrillation showing a diastolic pressure gradient across the tricuspid valve a rather slow *y* descent and absence of the *y* trough

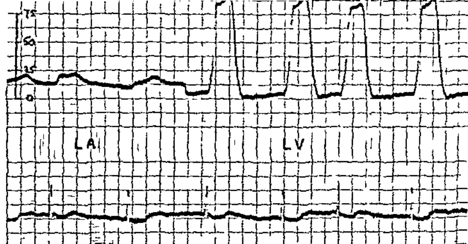
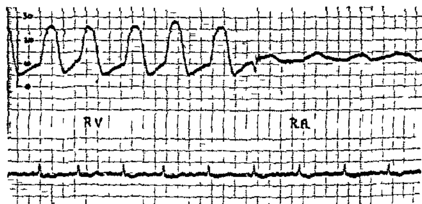
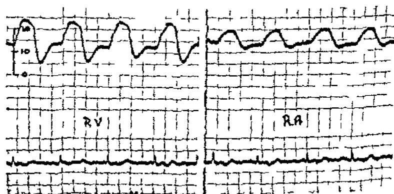



Fig 10.46—Pressure pulses from the left atrium and left ventricle in a case of mitral stenosis with atrial fibrillation showing a diastolic pressure gradient across the mitral valve slow y descent and absent y trough




Tricuspid stenosis pre operative




Post operative tricuspid incompetence

Fig 10.47—Pressure pulses from the right ventricle and right atrium in a case of tricuspid stenosis before and after tricuspid valvotomy The slow y descent and absent y trough have been abolished

is seen with normal rhythm the diastolic with atrial fibrillation Filling of the right ventricle is retarded so the rate of *v* descent following *v* in right atrial and jugular pressure pulses is relatively slow (fig 10 47) and there is no appreciable *y* trough (Gibson and Wood 1955) The change in the slope of *y* and the development of a *y* trough following surgical relief of the obstruction is well shown in the lower tracing of figure 10 47 (tricuspid incompetence was produced inadvertently in this case) The size of the orifice may be calculated from the cardiac output pressure gradient and heart rate as described for mitral stenosis

The right atrium becomes hypertrophied and distended while the right ventricle remains quiet underfilled and small The low cardiac output high venous pressure and distended liver encourage œdema and ascites as in Pick s disease, which in some respects it resembles (Thompson and Levine 1937)

## CLINICAL FEATURES

There were 16 women and 6 men in my small series of 22 cases Their average age was 35 the range 21 to 48 Figures from the literature are not included because up till now the majority of mild and moderate cases have been overlooked clinically Necropsy figures however show that the average age and sex ratio in tricuspid cases is much the same as for mitral stenosis (Aceves and Carral 1947)

### *Symptoms*

The first symptom may be fluttering discomfort in the neck caused by the development of a giant *a* wave in the jugular pulse More often the pulse is seen in the mirror or noted by an interested relative Hepatic pulsation is rarely mentioned by the patient

Apart from this there are no complaints attributable to tricuspid stenosis until the cardiac output is sufficiently reduced to cause fatigue or the liver sufficiently enlarged to cause obvious swelling of the abdomen œdema and ascites follow At the same time the patient is usually spared the distressing symptoms that would otherwise have developed on account of the associated mitral stenosis thus hæmoptysis acute pulmonary œdema paroxysmal cardiac dyspnœa orthopnœa and winter *bronchitis are* noticeably absent in the majority of cases

### *Physical signs*

There are so many characteristic and specific features of tricuspid stenosis that it is remarkable how frequently the clinical diagnosis is over looked In fact a confident bedside diagnosis can be made in 80 per cent of cases if proper attention is paid to the following points

1 If there is normal rhythm there is almost invariably a *giant a wave* in the jugular pulse (fig 10 48) and *presystolic hepatic pulsation* as noted by Mackenzie (1902)

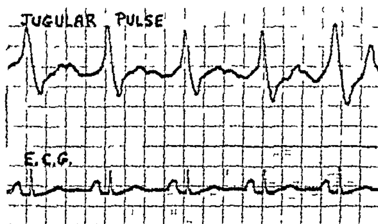



Fig 10 48—Jugular phlebogram showing giant *a* waves in a case of tricuspid stenosis with normal rhythm

2 If there is atrial fibrillation there is a prominent *v* wave in the jugular pulse which characteristically subsides slowly, *there is no y dip* (fig 10 47) as there is in all other conditions with venous pressures at this level (Owen and Wood 1955 Gibson and Wood 1955)

3 *The heart itself is quiet* there being no appreciable lift over the right ventricle as there usually is in pulmonary hypertensive cases of mitral stenosis which may also cause giant *a* waves in the jugular pulse Pulmonary valve closure is also impalpable

Expiration Inspiration

Fig 10 49—Phonocardiogram showing the effect of inspiration on the tricuspid atriosystolic murmur The prominent *a* wave in the jugular phlebogram also increases with inspiration

4 *Auscultation* at the left sternal edge in the fourth space reveals a tricuspid presystolic or diastolic murmur which is sharply accentuated during inspiration (fig 10 49) when right ventricular filling is encouraged (Carvallo 1950) A thrill may accompany the bruit A tricuspid opening snap may also be heard (Kossman 1955) but may be difficult to distinguish from the mitral opening snap which is usually present unless it is accentuated during inspiration Accentuation of the tricuspid first sound also increased by inspiration is even less convincing An associated tricuspid systolic murmur may be present but is far from invariable The pulmonary component of the second heart sound is not accentuated as in pulmonary hypertensive cases of mitral stenosis and there is never right atrial presystolic gallop which usually accompanies the giant *a* wave in other conditions

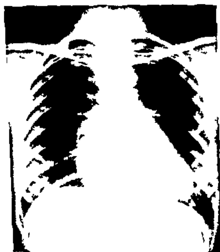


Fig 10 50—Skiagram from a case of tricuspid stenosis showing conspicuous enlargement of the right atrium without dilatation of the pulmonary artery note also the absence of pulmonary venous congestion

5 *Fluoroscopy* shows characteristic enlargement of the right atrium without conspicuous dilatation of the pulmonary artery and the lung fields are relatively clear (fig 10 50) Absence of enlargement of the right ventricle is difficult to demonstrate radiologically when the right atrium is dilated Calcification of the tricuspid valve is very rare

6 The *electrocardiogram* in cases with normal rhythm commonly shows the highly characteristic combination of an unusually tall widened P wave (combined P pulmonale and P mitrale) and absence of right ventricular preponderance (fig 10 51)

## DIFFERENTIAL DIAGNOSIS

The possibility of tricuspid stenosis should be borne in mind in any case of mitral valve disease in which the jugular venous pressure is unquestionably raised the differential diagnosis then lying between this, uncontrolled atrial fibrillation severe mitral incompetence a high pulmonary vascular resistance and pericardial effusion for in uncomplicated mitral stenosis the venous pressure is nearly always normal a primary myocardial fault being rare (Wood 1954)

Digitalis soon controls the ventricular rate and allows the jugular pulse to be analysed more easily Mitral incompetence should be recognised



Fig 10 51—Electrocardiogram showing exceptionally tall yet widened P waves in a case of mitral and tricuspid stenosis Note also the absence of right axis deviation

without difficulty and if severe the likelihood of associated tricuspid stenosis is remote If a high pulmonary vascular resistance is responsible for the giant *a* wave it should be recognised by the heaving right ventricle accentuated pulmonary second sound conspicuously dilated pulmonary artery and strong right ventricular preponderance electrocardiographically Pericardial effusion may have to be considered but it does not cause a giant *a* wave slow *y* descent nor absent *y* trough radiologically the app arances can be similar but the P wave of the electrocardiogram is normal when there is sinus rhythm Pathognomonic of tricuspid stenosis are the slow *y* descent and tricuspid bruits

Ebstein s disease certain cardiopathies usually of unknown or uncertain etiology and chronic constrictive pericarditis may bear *some superficial resemblance to rheumatic tricuspid stenosis but their distinction is rarely difficult* They are *more* likely to be confused with isolated tricuspid stenosis *from disseminated* lupus

## *SPECIAL TESTS*

*Cardiac catheterisation* is the most convincing way of proving or disproving *the existence of physiological tricuspid* stenosis By sliding the tip of a *looped* catheter up and down the lateral wall of the right atrium pericardial effusion can be easily diagnosed or eliminated After recording left atrial and pulmonary artery pressures and measuring the cardiac output

in the usual way the catheter is withdrawn slowly from the right ventricle to the right atrium while intracardiac pressures are recorded continuously In normal controls the diastolic and presystolic right atrial pressure is identical with the right ventricular diastolic and end diastolic pressure respectively (fig 10 5-) whereas in tricuspid stenosis a presystolic or diastolic pressure gradient across the valve can be demonstrated routinely (fig 10 53 and 10 47) If by ill fortune the right ventricle cannot be entered the slow y descent in the right atrial tracing should still reveal the correct diagnosis The Rv/v ratio has not yet been worked out for tricusp d valve disease

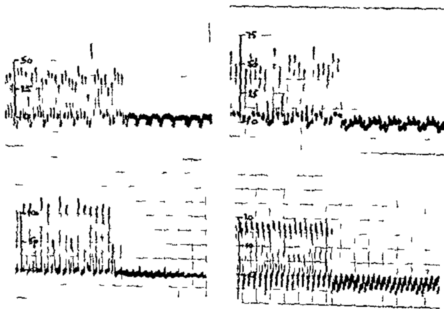


Fig 10 5 —Withdrawal tracings from right ventricle to right atrium showing identical diastolic pressures in these two chamber in four controls

*Phonocardiography* confirms the tricuspid origin of the murmurs and demonstrates their relationship to respiration (fig 10 49)

## *PROGNOSIS*

It has long been known that some patients with obvious tricuspid stenosis may carry on their occupations for a remarkably long time with relatively little disability On the other hand others linger on year after year in considerable distress from fatigue chronic œdema ascites and distended abdomen whether they attempt to continue a sedentary occupation or not A rigid low sodium diet repeated injections of *mersalyl* and occasional abdominal paracentesis may relieve these symptoms but not without adding their own discomforts

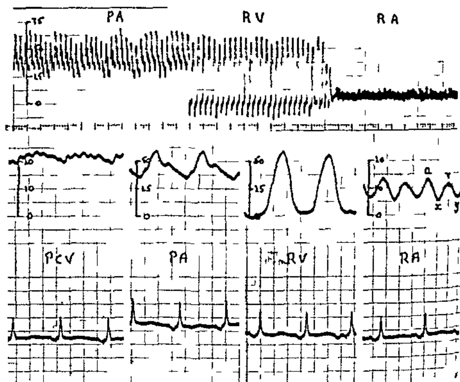



Fig 10 53—Withdrawal tracings from the right ventricle to the right atrium in a case of tricuspid stenosis with normal rhythm showing a presystolic and diastolic pressure gradient across the tricuspid valve

Aceves and Carral (1947) found that life expectancy averaged five years from the time the diagnosis was first made but in the past the diagnosis has been made notoriously late Thompson and Levine (1937) particularly have emphasised the relatively long life expectancy and surprising ability of patients to carry on despite the discomforts and gross physical signs alluded to above

## *TREATMENT*

Medical measures include all the usual means of combating chronic ascites and œdema prior to their onset however the patient should not be unduly restricted for there is little danger of acute pulmonary congestive symptoms despite coincident mitral stenosis

*Tricuspid valvotomy* has only been undertaken in a few isolated cases so far (Trace *et al* 1954 Chesterman and Whittaker 1954 O Neill Janton and Glover 1954 McCord Swan and Blount, 1954) There may be considerable difficulty in locating the commissures and serious tricuspid incompetence may result from too bold an attack as in the patient whose tracings are illustrated in figure 10 47 In the great majority of my own cases the tricuspid stenosis was not severe enough to warrant interference although mitral valvotomy was carried out in several of them

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CHAPTER XI

# NON-RHEUMATIC MYOCARDITIS AND MISCELLANEOUS CARDIOPATHIES

UNDER this heading are grouped together all those varieties of heart disease that have in common a primary or predominant myocardial fault That only one chapter should be devoted to what might appear to be the very essence of cardiology emphasises the curious fact that the great majority of so called diseases of the heart are simply those conditions that hinder filling mechanisms increase cardiac work or interfere with fuel supplies i e mechanical disadvantages of one kind or another What greater compliment could be paid to the general health and integrity of the myocardium itself than this?

### *Incidence*

At present no definite figure can be given for the prevalence of non rheumatic myocarditis and clinically similar cardiopathies, for there are wide discrepancies between clinical instrumental and pathological data

However out of approximately 10 000 new patients with cardiovascular disease examined personally by the author only 30 were in this category excluding cases of diphtheria thyrotoxicosis myxœdema and digitalis or quinidine intoxication This gives a relative clinical frequency of 0 3 per cent for cases presenting like isolated myocarditis

### *Age and sex*

The average age of the patients in this series was 44 the range 14 to 63 but a primary myocardial fault may occur at any age In infants a congenital cause such as fibroelastosis von Gierke s disease or anomalous origin of the left coronary artery from the pulmonary artery is more likely

The male/female sex ratio was 2 1

### *Classification*

The group comprises numerous infections and infestations the collagen diseases and allied allergic states disorders of metabolism or nutrition certain endocrine disturbances neuro muscular dystrophies primary or secondary tumours of the heart and a number of drugs and poisons included also are at least two important cardiopathies of unknown origin—isolated myocarditis and endomyocardial fibrosis For convenience a list of the more important members of each sub group is given below

## ETIOLOGY

*Bacterial infections*
1 Invasive
- Pyogenic organisms
- Syphilis

2 Toxic
- Bacterial endocarditis
- Diphtheria
- Meningococcal septicæmia
- Pneumonia
- Streptococcal infections
- Tuberculosis
- Typhoid fever
- Typhus (especially scrub typhus)

*Fungus or yeast infections*
- Actinomycosis
- Coccidioidomycosis
- Histoplasmosis

*Parasitic or protozoal infections*
- Bilharziasis
- South American trypanosomiasis (Chagas disease)
- Toxoplasmosis
- Trichiniasis

*Virus infections*
- Common cold
- Infective mononucleosis
- Influenza
- Mumps
- Poliomyelitis

*Collagen diseases*
- Dermatomyositis
- Disseminated lupus
- Periarteritis nodosa
- Rheumatoid arthritis
- Scleroderma

*Congenital anomalies*
- Anomalous left coronary artery
- *Familial cardiomegaly*
- Fibroelastosis
- Friedreich s disease
- Gargoylism
- Von Gierke s disease

*Drugs*
- Adrenalin
- Calcium
- Digitalis
- Emetine
- Potassium
- Quinidine

*Endocrine disorders*
- Acromegaly and gigantism
- Myxœdema
- Thyrotoxicosis

*Metabolic or nutritional disorders*
- Alcoholism
- Amyloidosis
- Beri beri
- Diabetes mellitus
- Hæmochromatosis
- Malnutrition

*Neuromuscular dystrophies*
- Progressive muscular dystrophy

*Tumours*
- Fibroma
- Leukæmia
- Myxoma
- Rhabdomyoma
- Sarcoma
- Secondary tumours
- Argentaffinoma

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*Isolated myocarditis*
- Endomyocardial fibrosis
- Fiedler s type

*Allergic or other tissue reactions*
- Loffler s syndrome
- Sarcoidosis

### *Hæmodynamics*

The chief physiological fault common to nearly all groups is inability on the part of the weakened myocardium to maintain an adequate cardiac output despite normal pressure and volume loads normal coronary flow and normal rhythm Hypertrophy of relatively healthy muscle fibres a high filling pressure in both venous systems giving increased diastolic stretch, and tachycardia may compensate for the defect for a while but

sooner or later prove inadequate one or other or both ventricles becoming overloaded

## BACTERIAL INFECTIONS

The great majority of cases of myocarditis secondary to bacterial infection are toxic and the best example is diphtheritic myocarditis Bacteria may actually invade the myocardium however in certain instances e g in syphilitic myocarditis (q v ) and suppurative myocarditis Miliary or solitary abscesses of the myocardium may occur in staphylococcal or pneumococcal septicæmia and may cause purulent pericardial effusion or cardiac rupture (Weiss and Wilkins 1937) The outlook in these previously fatal cases has altered considerably since the advent of penicillin and other antibiotics

## THE HEART IN DIPHTHERIA

Diphtheria may cause peripheral circulatory collapse or toxic myocarditis Cutaneous diphtheria so easily overlooked and so often untreated until too late may be as lethal as the common faucial type Early and adequate treatment with antitoxin has greatly reduced the *incidence of* toxic complications but has by no means abolished them Experimentally in dogs diphtheria toxin causes peripheral vasodilatation conduction defects and weakness of myocardial contraction ending in failure (Witt Lindner and Katz 1937)

### *CIRCULATORY COLLAPSE*

Towards the end of the first week or during the second week of the illness the blood pressure may fall well below 100 mm Hg the *patient* becomes faint sick and restless the skin pale cold and clammy the pulse rapid and thready Loss of vasomotor tone may be due to toxic depression of the vasomotor centre perhaps to peripheral *sympathetic paresis,* or possibly to poisoning of the vessels themselves Occasionally *it is brought* about by suprarenal failure due to necrosis or hæmorrhage The earlier the onset of circulatory collapse the worse the prognosis Patients *usually* re main in a critical state for several days in those who recover improvement may then occur but the blood *pressure usually* remains low for two or three weeks

The course of diphtheria may be *complicated* (as *well* as alleviated) by serum therapy for this may induce not *only immediate* collapse from anaphylactic shock in a sensitised individual *but also later collapse* from loss of plasma into the tissue spaces associated with serum sickness Urticaria and œdema usually *on the* ninth day may be extreme and result in a diminished blood volume and hæmoconcentration Diphtheritic circulatory collapse and allergic *shock* may thus be expected at about the same time and diagnostic difficulties may arise

*Treatment of serum sickness* includes subcutaneous adrenalin 0 5 mg two to four hourly sodium salicylate gr 15 to 20 (1 to 1 25 G) three hourly and one of the anti histamine drugs such as diphenhydramine (benadryl) 50 mg six hourly

*Treatment of diphtheritic circulatory collapse* consists of raising the foot of the bed and maintaining the blood pressure by means of a slow drip infusion of some suitable pressor amine such as noradrenalin, at a rate of about 5 to 15 μg per minute In view of the uncertain state of the myo cardium in these cases too much saline must not be given and the blood pressure should not be raised above 120 mm Hg It is best to use a strength of 1 mg of noradrenalin to 100 ml of normal saline 15 drops (1 ml) of such a solution per minute should contain 10 μg of noradrenalin Alterna tively mephentermine may be given intramuscularly in doses of 25 to 50 mg (usually 30 to 35 mg) and repeated when necessary or mephenter mine may be given by slow intravenous drip at a rate of 0 5 to 1 mg per minute until the blood pressure is satisfactory

The *prognosis* is grave

## TOXIC MYOCARDITIS

*Pathology* Diphtheritic carditis being toxic in nature may prove fatal without causing advanced changes in morbid histology The characteristic finding is hyaline degeneration or necrosis of muscle the fibres losing their striations and presenting a swollen granular appearance Lesions are patchily distributed and only short segments of individual muscle fibres may be affected Monocytes cluster round the debris and fibroblastic repair follows (Gore 1948)

*Clinical features* Disturbances of rhythm tend to occur first usually during the second week of the disease Partial or complete heart block and bundle branch block are the best known and in patients who recover from the illness are usually but not invariably transient (Perry, 1939) Both heart block and bundle branch block commonly denote severe carditis most such cases proving fatal (Burkhardt Eggleston and Smith 1938) Ectopic beats are common and although often innocent and unrelated to carditis should be viewed with suspicion in diphtheria Auricular fibrilla tion and paroxysmal tachycardia are rare Ventricular fibrillation may be responsible for sudden death

Other evidence of carditis tends to occur a little later usually during the third week Sinus tachycardia gallop rhythm enlargement of the heart and reduction of the pulse pressure are usual The onset of heart failure may be suggested by pallor breathlessness præcordial oppression and vomiting Congestion is systemic rather than pulmonary the jugular venous pressure being raised and the liver distended there is rarely orthopnœa paroxysmal cardiac dyspnœa or pulmonary œdema Significant murmurs and peri cardial friction are absent

The *electrocardiogram* is especially helpful in the diagnosis of diphtheritic carditis much more so than in rheumatic carditis Depression of the RS T segment or primary inversion of the T wave in most leads is characteristic and is found during the second week in the majority of cases which develop clinical carditis and in some that do not A similar pattern may be produced in cats within 48 hours by injecting diphtheritic toxin (Nathanson 1928) Of 600 cases of diphtheria studied by Altshuler *et al* (1948) 108 or 18 per cent developed these changes while only 11 showed heart block

Radiological studies on diphtheritic carditis are rare because patients are not allowed to stand or sit, and should not be moved to the X ray department Portable skiagrams give little information about the size of the heart General dilatation however may be expected if the venous pressure is raised

*Prognosis* The outlook is grave for sudden death is common and presumably results from ventricular fibrillation or asystole Some patients die from congestive heart failure Not infrequently associated circulatory failure complicates the picture Those who survive usually develop polyneuritis later and this is apt to be severe The total mortality rate is difficult to assess for mild cases may well be overlooked but it is usually put at 50 per cent

If the patient survives the ultimate prognosis is excellent (White *et al* 1937) and complete recovery may be promised without reserve It is important that the patient should be convinced of this from the start in order to prevent anxiety neurosis and to maintain good morale

*Treatment* Antitoxic serum will already have been administered in most cases if not it is too late to give it by the time cardiovascular symptoms develop The axiom that antitoxin cannot do any harm and might as well be given even at this stage is untrue for serum reactions are common and may prove fatal when there is toxic circulatory collapse or carditis

Prophylactic treatment in addition to early and adequate doses of antitoxin consists of complete rest in bed for a minimum period of one month in all cases of diphtheria If by the end of this time there is no evidence of cardiovascular or neuro intoxication there is little further risk to life Should any such intoxication have occurred however bed rest must be extended for another month otherwise sudden death may occur during convalescence in the second month Patients may be treated with far less respect subsequently even when they have extensive polyneuritis

The treatment of recognised carditis is unsatisfactory Absolute rest is essential for sudden slight effort even sitting up in bed may prove fatal during the critical period Patients should be nursed flat with one pillow and should have everything done for them including being fed and washed

Diet should be light and fluids limited to two pints daily If there is congestive failure the sodium intake should not exceed 0 5 G daily

Digitalis is dangerous and should only be used in rare cases when atrial fibrillation with a rapid ventricular rate is associated with severe congestive heart failure Quinidine is also dangerous in view of its depressive effect on conduction

## THE HEART IN OTHER INFECTIONS

Up to the beginning of the twentieth century it was generally believed that toxic carditis was a common complication of certain fevers such as influenza It came to be recognised however that although cloudy swelling and 'fatty degeneration were often found at autopsy in cases dying from severe general infections clinical evidence of cardiac involvement was rare The change of view followed the establishment of stricter criteria for diagnosing organic heart disease palpitations and irregularities of the heart were shown to be due to autonomic disturbance or to innocent ectopic beats systolic murmurs lost their previous significance, effort syndrome following infections was proved attributable to anxiety X rays failed to confirm clinical cardiac enlargement (based on the position of the apex beat) standard lead electrocardiograms were rarely abnormal The weight of negative evidence was considerable and it became the custom to recognise no form of carditis other than that due to rheumatism or diphtheria In recent years however the earlier view has gained some support particularly owing to the work of Gore and Saphir (1947) who found that diphtheria and rheumatism accounted for less than 25 per cent of fatal cases of myocarditis they contended that carditis was common in a host of infectious diseases including especially scrub typhus bacterial endocarditis and meningococcal septicæmia It may be as well therefore to review the known facts critically for there is grave danger that this modern swing back may go too far

### *FAILURE OF THE PERIPHERAL CIRCULATION*

Cardiovascular disturbances in acute infections are commonly of two kinds and neither is due to a cardiac fault The first is peripheral circulatory failure This may be due to depression of the vasomotor centre to toxic paresis of the vessels themselves to suprarenal failure or to diminution of the blood volume from dehydration or from loss of plasma into the tissue spaces through damaged vessels The essential mechanism is critical discrepancy between the effective vascular capacity and the blood volume so that the central venous pressure falls the cardiac output is reduced and the blood pressure low as in shock

A good sign of vascular relaxation is a markedly dicrotic pulse and although not necessarily serious should put the physician on guard Another significant feature is pallor and coldness of the extremities due to vasoconstriction in the skin this appears to be a compensatory mechanism helping to maintain the venous pressure and blood pressure when dangerous vasodilatation occurs elsewhere e g in muscle Impending failure

of compensatory vasoconstriction may be indicated by waxing and waning of the systolic blood pressure through a range of 10 to 20 mm Hg A fourth indication of circulatory failure is mental confusion or faintness in the sitting posture Whilst tachycardia is the rule and the half hourly pulse chart of some value it should be understood that deceleration sometimes accompanies a falling blood pressure and that the character of the pulse is as important as its rate

Circulatory failure should be treated by nursing the patient flat or with the foot of the bed raised and by the intravenous administration of serum or plasma by the drip method with or without noradrenalin in doses of about 10 $\mu$g per minute

The second common cardiovascular reaction to acute fevers is vasomotor neurosis during convalescence This is discussed in Chapter XXII

## *TOXIC MYOCARDITIS*

True toxic myocarditis does occur however especially perhaps in pneumonia Sections reveal focal hyaline necrosis i e granular degeneration and loss of striation of the muscle fibres patchily distributed Cellular reaction with monocytes predominating and fibroblastic repair follow—as in diphtheritic carditis which it resembles This histological picture is common to most forms of carditis—hence the difficulty in making an etiological diagnosis from autopsy findings For example 35 cases of sudden death following tonsillitis or common cold were reported by Gore and Saphir (1947) and ascribed to toxic myocarditis Thirty one of them however could have been due to diphtheria or pneumonia a negative throat swab does not exclude diphtheria

Myocarditis and diffuse glomerulonephritis have long been known to complicate bacterial endocarditis but when the death rate of the septicæmic stage was 98 per cent they received scant attention Since the introduction of penicillin however heart failure from myocarditis has been said to be chiefly responsible for the present 25 per cent mortality nevertheless heart failure is rare in the absence of severe aortic or mitral incompetence and the rapidly progressive mechanical fault could well be to blame

Histological examination of the heart in cases dying from meningococcal infection may disclose evidence of carditis but clinical signs of cardiac involvement are most unusual and the total mortality rate in adults is less than 1 per cent (Daniels *et al* 1943)

*Pneumococcal* and *streptococcal* myocarditis accompanying pneumonia and scarlet fever respectively are perhaps the most convincing forms of non diphtheritic bacterial toxic myocarditis especially the former Streptococcal myocarditis of this kind bears no resemblance to rheumatic carditis which is a more likely complication of scarlet fever

*Tuberculous* myocarditis sometimes accompanied by erythema nodosum has been reported in association with primary tuberculosis (Neidhart and Rumrich 1950) but is believed to be allergic in type Six out of 30 cases

of otherwise idiopathic myocardial fibrosis described by Perrin Froment and Lenegre (1953) had pulmonary or mediastinal tuberculosis

Collapse in *typhoid fever* is usually due to peripheral circulatory failure evidence of true myocarditis being unconvincing (Porter and Bloom, 1935) Electrocardiographic changes during the course of typhoid have been reversed within 48 hours of giving 300–600 mg of niacin (nicotinic acid) daily by mouth (Rachmilewitz and Braun 1948) suggesting deficiency of at least one of the B group of vitamins

Carditis accompanying scrub typhus (Tsutsugamushi fever) is clinically unconvincing Although histology may reveal myocardial damage and cellular infiltration in fatal cases (Corbett, 1943) the clinical course of the disease seems to be little influenced by them (Williams *et al* 1944 Berry *et al* 1945) In a series of 184 cases seen within one to four weeks after the acute symptoms had subsided and 10 cases seen during the stage of fever the electrocardiogram was virtually normal (Howell 1945) For further information the reader is referred to the issue of the *American Journal of Hygiene*, May 1945 which is devoted to studies on scrub typhus

Certain *virus infections* are known to cause myocarditis occasionally these certainly include infective mononucleosis mumps and poliomyelitis Saphir (1949) gives a much longer list and includes infective hepatitis and virus pneumonia In the war however I encountered no clinical example of myocarditis associated with infective hepatitis or virus pneumonia despite having well over a thousand cases of the former and nearly 300 of the latter under my care This discrepancy between clinical and pathological data permeates the whole subject In poliomyelitis for example Ludden and Edwards (1949) found microscopic evidence of myocarditis in 14 out of 35 fatal cases whereas Spain *et al* (1950) reported only one instance of clinical myocarditis in 140 cases although typical microscopic changes were found in 12 out of 14 that were fatal I have however seen unquestionable examples of clinical myocarditis in adults associated with glandular fever and mumps

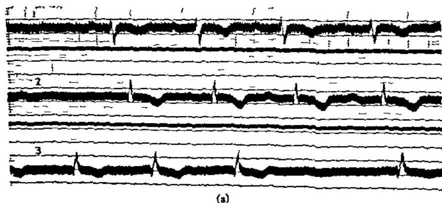
The common cold influenza and other upper respiratory tract infections have been held responsible for many cases of alleged myocarditis but the rarity of any such complication is much more impressive considering the frequency of these maladies in a widespread epidemic of influenza in which clinical evidence of myocarditis was carefully sought, no single example could be found (Wood 1941)

To assess the clinical value of the work of Gore and Saphir quoted above it is worth noting that 16 per cent of their 1 402 cases of myocarditis were due to scrub typhus and there was no evidence that myocarditis was the cause of death Their cases were highly selected excluded children and were based entirely on autopsy findings there were 227 examples of scrub typhus 208 of bacterial endocarditis 144 of diphtheria 130 of rheumatic carditis and 105 of sulphonamide allergy The reader will draw his own conclusions

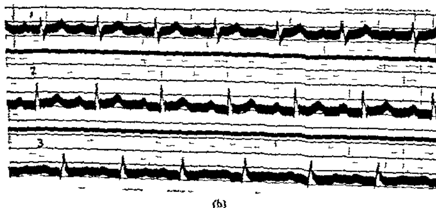
Clinically significant carditis accompanying acute infections in Great Britain (other than rheumatic fever diphtheria and bacterial endocarditis) is undoubtedly rare

*Clinical features of toxic myocarditis* In acute cases the signs and symptoms are similar to those of diphtheritic myocarditis, except that they may occur earlier during the febrile stage of the infection Symptoms attributable to cardiac involvement may be absent on the other hand there may be dyspnœa unexpected *vomiting* pallor and peripheral cyanosis due to congestive failure substernal oppression or discomfort or palpitations associated with changes of rhythm It may be difficult to distinguish cardiac symptoms from those due to general toxæmia particularly when there is peripheral circulatory failure Sudden death is not infrequently the first tragic proof of myocarditis

Physical signs include a small rapid thready pulse low systolic blood pressure small pulse pressure gallop rhythm dilatation of the heart,




(a)




(b)

FIG 11 01—Electrocardiogram in a case of toxic myocarditis due to pneumonia
(a) Shows partial heart block with dropped beats and inversion of the T wave in all leads
(b) After recovery

congestive heart failure abnormalities of rhythm and electrocardiographic changes The small rapid pulse and the low blood pressure may equally well be due to peripheral circulatory failure and the gallop rhythm to fever (especially when there is anæmia) The size of the heart may be difficult to assess under the clinical circumstances and the patient should not be moved to the X ray department for more exact information The importance of recognising early signs of congestive heart failure will thus be appreciated Abnormalities of rhythm are also important and include all grades of heart block auricular flutter or fibrillation and paroxysmal tachycardia The electrocardiogram is especially helpful not only in establishing the nature of a rhythm change but also in revealing partial heart block and abnormalities of the T wave (fig 11 01)

Sometimes the course of toxic myocarditis is subacute or chronic The clinical features then closely resemble those of isolated myocarditis (q v)

*Prognosis* If the diagnosis is beyond doubt the outlook is grave, the mortality rate probably approaching 50 per cent Whether central or peripheral in mechanism the combination of hypotension and a small rapid pulse is always dangerous and congestive heart failure often proves fatal Abnormalities of rhythm and alterations of the T wave without the manifestations just mentioned are less serious

Many cases of mild toxic myocarditis must pass unrecognised but this is not a matter for concern for recovery appears to be complete in all non fatal cases

*Treatment* Bed rest and specific chemotherapy (when applicable) for all acute infections are axiomatic bed rest should be absolute if the cardio vascular system is involved The patient should be nursed in the position of maximum comfort but if the blood pressure is below 100 mm Hg and there is no evidence of congestive failure he should be kept horizontal if there is congestive failure he should be propped up at 30 to 45 degrees against a back rest Digitalis should be avoided unless there is frank congestive failure for it increases the risk of sudden death from ventricular fibrillation and may aggravate minor degrees of heart block If the venous pressure is well raised and the liver distended however it should not be withheld and it may be invaluable in ca es of auricular flutter or fibrillation Mersalyl and a low sodium diet may be given if there is fluid retention Quinidine or procaine amide may have to be used in cases of paroxysmal ventricular tachycardia but its depressive effect on conduction can be very dangerous if there is already partial heart block

It must be admitted however that toxic myocarditis is little influenced by therapy and is apt to be fatal or otherwise according to its severity

## MYOCARDITIS DUE TO PARASITES

A most convincing form of protozoal myocarditis may accompany *South American trypanosomiasis* or Chagas disease (Chagas 1909) Leish

manial forms of *T cruzi* multiply chiefly in the cells of the heart brain and liver the affected cells finally rupture and liberate the parasites into the blood stream An intense local inflammatory reaction follows The signs and symptoms of a typical acute or subacute myocarditis may dominate the clinical picture and sudden death is common (Mosely and Miller 1945) The clinical diagnosis may be suggested by associated encephalitis and may be proved by demonstrating the parasites in the blood stream

Of the protean manifestations of *toxoplasmosis* myocarditis must be relatively rare but three cases have been reported recently by Paulley *et al* (1954) and others may come to light now that serological tests are likely to be performed in cases of myocarditis of uncertain etiology The protozoal intracellular parasite known as toxoplasma seems to be far more widespread in man than originally suspected but the majority of individuals with positive serological tests give no indication of disease The best known clinical reactions are cerebral and ophthalmic whether congenital or acquired (Vail *et al* 1943 Ridley 1949) If there is a myocardial reaction however a clinical picture resembling that of isolated myocarditis may arise or myocarditis may complicate more familiar manifestations of the disease The diagnosis is strongly supported by a specific complement fixation test at titres of 1/16 or higher

*Trichiniasis* is rarely complicated by myocarditis, and even minor electrocardiographic abnormalities are uncommon Thus of 44 cases investigated by Beecher and Amidon (1938) only one had a slightly prolonged P R interval and one sino auricular block Solarz (1947) found transient flat or inverted T waves in 16 out of 114 cases (14 per cent) but no clinical evidence of myocarditis in any of them Allergic reactions to trichiniasis occur however and rare instances of myocarditis may perhaps be of this kind

*Schistosomiasis* is more likely to affect the heart by causing pulmonary hypertension from obliterative pulmonary endarteritis than myocarditis although I have seen a pathological specimen of the latter in South Africa Cor pulmonale due to bilharzia is described in chapter XVIII

There is little evidence that *malaria* causes myocarditis collapse is usually due to peripheral circulatory failure

A *hydatid cyst* may be found in the heart or pericardium as a result of a routine skiagram of the chest but is rarely recognised clinically unless it ruptures This is a *space filling lesion* rather than a myocarditis The electrocardiogram may show reduced R waves and inverted T waves in chest leads taken from points overlying the cyst Rupture may be into the pericardial sac or into any of the cardiac chambers (Canabal *et al* 1955) The differential diagnosis is from other pericardial cysts cardiac tumours mediastinal cysts and neoplasms and cardiac aneurysm Echinococcal cysts elsewhere the Casoni test and the complexion fixation test help to establish the diagnosis

## MYOCARDITIS DUE TO FUNGI AND YEASTS

*Actinomycosis* involves the heart in less than 2 per cent of cases (Kasper and Pinner, 1930) When it does so the fungus usually reaches the heart by direct extension from infected neighbouring structures, so that pericarditis occurs first, but initial myocarditis from hæmatogenous spread has also been reported (Cornell and Shookhoff 1944) Clinically, the majority of cases have been recognised owing to the development of congestive heart failure, signs of pericarditis have been detected less frequently Treatment includes heavy and prolonged doses of sulphonamides penicillin and surgery (Lyons *et al* 1943 Zoeckler 1951)

Myocardial *coccidioido mycosis* was found in 11 out of 48 cases included in the series reported by Gore and Saphir (1947) Clinically, however myocardial involvement is rare Thus in a large epidemic of 75 cases described by Goldstein and Louie (1943), all but one recovered without evidence of carditis In this group the incubation period was 14 days Symptoms and signs included fever pleurisy cough with brownish or blood stained sputum, cervical adenitis erythema nodosum or multiforme and bilateral hilar opacities extending outwards into the central zone of the lungs Leucocytosis, eosinophilia and a high sedimentation rate were the rul The diagnosis can be confirmed by a specific skin sensitivity test a complement fixation test and by identifying the fungus in the sputum

*Histoplasmosis* is sometimes mentioned as a cause of myocarditis by yeast like organisms, but in a review of 71 cases Parsons and Zarafonetis (1945) found little evidence to support this statement There were four instances of vegetative endocarditis, two of them involving the tricuspid valve but no convincing examples of frank myocarditis

## ISOLATED MYOCARDITIS

Isolated myocarditis (Scott and Saphir, 1929) is a subacute or chronic inflammation of the heart of unknown etiology characterised by patchy myocardial necrosis cellular infiltration and fibroblastic repair, as in other forms of myocarditis *It was first properly described by Fiedler (1899)* The disease may not be a specific entity and is difficult to distinguish pathologically from known forms of toxic or infective myocarditis of relatively long duration

*Incidence* Although still relatively rare isolated myocarditis is being recognised with increasing frequency The majority of cases have occurred in subjects between the ages of 20 and 50 but infants children and old people are not exempt The disease has been reported sporadically in most countries and races and accounts for about half of all cases that present clinically with heart failure of unknown etiology

*Pathology* Patchy necrosis of muscle is thought to be the primary lesion (fig 11 02) Cellular reaction may be focal or more diffusely interstitial



(a)



(b)

Fig 11 02—Focal necrosis in a case of Fiedler's carditis

(a) Low power

(b) High power The cells are macrophages plasma cells lymphocytes and eosinophils

*(By courtesy of Prof C L Harrison)*

Monocytes predominate but in the acute stage polymorphs may be more numerous Hæmorrhage and exudate may occur Giant cells eosinophils and arteritis suggest another etiology—allergy Fibroblastic repair follows As a rule all stages of activity and healing are seen in the same specimen occasionally, extensive interstitial fibrosis is found alone and is believed to represents the end result of the same process As a rule these hearts weigh 500–600 G and are usually very dilated

The pericardium, endocardium and valves are not involved, but mural thrombi are common and may give rise to emboli and infarcts in other organs (Scott and Saphir 1929 Davies *et al* 1951)

*Clinical features* The history is invariably short, rarely longer than a few months The chief symptoms are increasing dyspnœa and fatigue, sometimes there is atypical angina pectoris or substernal discomfort (Hansmann and Schenken 1938) or an attack of pain may be so severe and prolonged as to suggest cardiac infarction (Gillis and Walters 1954) occasionally hemiplegia or hæmoptysis signals the onset (Josserand and Gallavardin 1901 de la Chapelle and Graef 1931)

The physical signs are usually those of congestive heart failure with a normal or low blood pressure small pulse pressure sinus tachycardia peripheral cyanosis and pallor cold extremities general enlargement of the heart (fig 11 03) gallop rhythm and normal valves Disturbances of rhythm particularly paroxysmal tachycardia atrial flutter and partial heart block are not uncommon

The *electrocardiogram* often shows left bundle branch block Not infrequently rather low voltage and simple inversion of the T waves in most leads may suggest Pick s disease Occasionally a relatively large zone of necrosis in the wall of the left ventricle may give rise to pathological Q waves and inverted T waves resembling the pattern of cardiac infarction In one case Bayley (1946) recorded typical anoxic depression of the RS T segment and attributed it to the fact that the lesions were mainly close to the endocardium of both ventricles

*Radiographic appearances* include moderate or considerable enlargement of the heart shadow particularly the left ventricle varying degrees of pulmonary venous congestion and dilatation of the right atrium and superior vena cava the aorta pulmonary artery and left atrium usually look normal

There is no fever, no leucocytosis no eosinophilia and no rise of sedimentation rate No special diagnostic tests are available

*Differential diagnosis* The case usually presents as one of heart failure of uncertain etiology It is at once distinguished from the *hyperkinetic circulatory states* (e g anæmia beri beri arteriovenous aneurysm Paget s disease of bone thyrotoxicosis anoxic pulmonary heart disease uræmia and certain diseases of the liver) by the obviously low cardiac output and signs of peripheral vasoconstriction

In middle aged or elderly subjects *ischæmic heart disease* may be difficult



Fig 11 03—Skiagram showing general enlargement of the heart in a case of Fiedler s myocarditis

to exclude if there is a history of angina pectoris or electrocardiographic evidence suggesting active ischæmia or an actual infarct In these unusual cases however, there is apt to be some discrepancy between the clinical situation and the suggested diagnosis of coronary disease for example there may be advanced congestive failure with minimal ischæmic changes in the electrocardiogram persistent heart failure may ante date pain the QT pattern suggesting infarction is rarely well developed and the S T segment is never conspicuously elevated A normal blood cholesterol and normal lipo proteins should add to the doubt

*Hypertensive heart disease* in which the blood pressure has temporarily fallen is seen occasionally but such a diagnosis should never be accepted readily without historical or subsequent proof (Kaplan Clark and de la Chapelle 1938)

*Aortic stenosis* with a minimal murmur heard best at the apex beat may be mistaken for isolated myocarditis with left ventricular failure and functional mitral incompetence The quality of the peripheral pulse an aortic ejection click the timing of the aortic murmur reversed splitting of the second heart sound (in the absence of left bundle branch block), and careful screening for calcium in the aortic valve should prevent error

*Pericardial effusion* may be closely simulated The apex beat however is usually more forceful in isolated myocarditis and much displaced to the left pronounced gallop rhythm points to a myocardial fault as does left bundle branch block Diagnostic paracentesis or cardiac catheterisation settles any lingering doubts

*Chronic constrictive pericarditis* without calcification can be clinically impossible to distinguish from isolated myocarditis, as emphasised by Davies *et al* (1951) A paradoxical pulse impalpable cardiac impulse and absence of gallop rhythm are all in favour of Pick s disease whilst a strong cardiac impulse functional tricuspid incompetence and left bundle branch block are all in favour of myocarditis but a small peripheral pulse high venous pressure steep *y* descent conspicuous *y* trough positive or negative Kussmaul sign absence of murmurs gallop rhythm T wave inversion maximal in leads $V_5$ and $V_6$ and moderate general enlargement of the heart shadow all occur frequently in both conditions *Routine cardiac catheterisation* does not distinguish them for in both the cardiac output is low left and right atrial pressures are high and more or less equal steep *y* descents followed by conspicuous *y* troughs and ventricular overshoots are seen on both sides of the heart and the pulmonary vascular resistance is normal (fig 11 04) Special physiological tests for distinguishing the two are under trial but have so far proved unreliable for cases of Pick s disease sometimes behave physiologically like cases of heart failure it is doubtful however if cases of heart failure ever behave like cases of uncomplicated Pick s disease The tests include direct measurement of change in cardiac output brought about by alterations in right ventricular filling pressure the

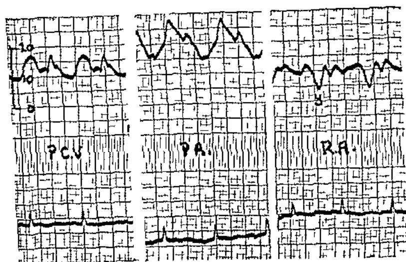



Fig 11 04—Pressure pulses from a case of isolated myocarditis showing high atrial pressures and a conspicuous *y* trough in the right atrial tracing

effect of Valsalva's manœuvre on the brachial arteriogram and the effect of change of posture on the digital pulse (see pages 292 and 293)

A *primary change of rhythm* particularly paroxysmal ventricular tachycardia in young persons or paroxysmal atrial flutter or fibrillation in later life may cause considerable diagnostic difficulty when attacks are prolonged recurrent and difficult to control for severe heart failure may well occur under such circumstances and if the patient is examined during a short period of normal rhythm there is likely to be a raised venous pressure gallop rhythm low blood pressure small pulse considerable cardiac enlargement and widespread inversion of the T waves in the electrocardiogram, it is easy then to assume that the rhythm change was secondary to myocarditis The life and future good health of the patient may well depend on a more enlightened view which is that every case of heart failure of uncertain etiology associated with an important change of rhythm should be regarded as secondary to that rhythm change until proved otherwise Every effort must be made to restore normal rhythm and to maintain it for at least six weeks, by the end of that time nutritional changes in the myocardium should have cleared up completely if the change of rhythm was primary

Once it has been concluded that the case is one of isolated myocarditis or one of the many other cardiopathies described in this chapter a serious attempt should be made to identify its nature This may involve much time and labour and the results are usually negative and disheartening but any other attitude must halt progress in this baffling field

*Course and prognosis* All proven cases have naturally been fatal even so, there have been no reports of probable cases that have survived Death

has usually occurred within a few weeks to a year or two of making the diagnosis or of admitting the patient to hospital

*Treatment* Absolute rest in bed digitalis, mercurial diuretics and a low sodium diet may help but the general response is poor Neither cortisone nor A C T H has proved of any value even in large doses

## ENDOMYOCARDIAL FIBROSIS

In recent years considerable interest has been aroused by an obscure cardiopathy characterised by extensive endocardial and subendocardial fibrosis When the endocardium is thick and white it resembles congenital fibroelastosis when the fibrosis is chiefly subendocardial the pathology is more like the most chronic form of isolated myocarditis or the most fibrotic form of nutritional cardiopathy described later It is therefore difficult to classify and until its etiology is understood it may be best to regard it as a special form of isolated myocarditis this at least emphasises our ignorance concerning its nature

The 40 cases in African troops serving in the Middle East described by Bedford and Konstam (1946) were having an adequate diet far better than they were accustomed to at home There were 17 necropsies in this series and the fibrosis was mainly subendocardial the authors thought the pathology resembled that of isolated myocarditis more closely than any other disease Davies (1948) described a very similar disease in 36 East African natives (32 male) at autopsy the heart was dilated rather than hypertrophied as in the series just quoted but the fibrosis involved the endocardium as well as the subendocardial myocardium The left ventricle was again chiefly involved and there was the same frequency of mural thrombosis as has been noted in nearly all forms of heart failure of obscure origin whether inflammatory allergic or nutritional A third series of 25 cases similar to Davies was reported by O Brien (1954) in the Sudan The diet was normal in 23 of them and alcoholism could be excluded The patients were older than the others averaging 54 years Functional mitral and tricuspid incompetence was stressed but it is doubted whether this had any special significance

Becker Chatgidakis and Van Lingen (1953) claimed that endomyocardial fibrosis was a diffuse collagen disease There were 32 Bantu subjects amongst their 40 cases but they did not blame the diet They also stressed cardiac dilatation rather than hypertrophy and the frequency of mural thrombosis The earliest lesion demonstrable was focal endocardial mucinous œdema similar lesions occurred as eccentric foci in the sub intimal tissues of the small blood vessels of the myocardium In addition interstitial myocardial œdema, attributed to increased capillary per meability, caused muscle bundles to be widely separated Fibrinous exuda tion was closely related to the areas of mucinous œdema and was the fore runner of mural thrombosis Foci of fibrinoid necrosis were seen in

well established areas of mucinous œdema In subacute cases cellular infiltration and granulomatous tissue appeared in the affected zones In chronic cases progressive fibrosis resulted in endocardial sclerosis myocardial fibrosis and eccentric subintimal connective tissue cushions' The authors thesis was that the general design of the changes described was characteristic of all collagen diseases

Clinically cases of endomyocardial fibrosis usually present as examples of heart failure of uncertain etiology Failure may be chiefly left sided or congestive Details are identical with those of isolated myocarditis

## COLLAGEN DISEASES AND ALLERGIC STATES

These include rheumatoid arthritis periarteritis nodosa disseminated lupus scleroderma dermatomyositis and Loffler s syndrome In all these conditions the clinical features of the cardiopathy closely resemble those of isolated myocarditis and will not therefore be discussed in detail again but each has specific features by which it may often be identified at the bedside or in the laboratory and these must be briefly described

*Rheumatoid arthritis*

Rheumatoid itself is too familiar to warrant detailed description here but it should be borne in mind that joint manifestations superficially resembling rheumatoid may occur in any of the collagen diseases particularly scleroderma

The heart may be involved in cases of rheumatoid in three different ways (1) chronic valve lesions indistinguishable from and probably identical with those following rheumatic fever are found in about 10 per cent (2) clinical pericarditis is not uncommon and necropsy evidence of healed pericarditis is found in 40 per cent of cases (3) a specific focal granulomatous myocarditis has been described by many authors in 1 to 3 per cent of cases (Sokoloff 1953) In addition severe secondary anæmia may affect the cardiovascular system

In differential diagnosis the following general rules may be found helpful in practice

1 Acute or subacute endocarditis in children with Still s disease and chronic valve lesions in adults with frank rheumatoid arthritis should be attributed to coincident or past rheumatic carditis respectively
2 Isolated pericarditis in children with Still s disease or in adults with rheumatoid may be attributed to the rheumatoid state with reasonable confidence but not to the neglect of excluding tuberculosis
3 A patient presenting with the combination of clinical rheumatoid arthritis and a cardiopathy resembling isolated myocarditis is more likely to have scleroderma or one of the other collagen diseases than true rheumatoid even cor pulmonale with secondary osteo arthropathy is more likely

*Periarteritis*

Periarteritis nodosa or polyarteritis is a manifestation of hypersensitivity (Rich 1942 Rich and Gregory, 1943) and may be provoked by a variety of antigens (Miller and Daley 1946) It is characterised by disseminated or patchily distributed segmental arteritis the initial lesion being fibrinoid necrosis of the media and internal elastic lamina cellular infiltration and secondary thickening of the intima Small aneurysms develop in about *16 per cent of cases (Harris Lynch and O Hara 1939) Serious disturbances* of function occur in the systems chiefly affected

*The disease may occur at any age but particularly in young adults and* is three times as frequent in males as in females

Cases tend to sort themselves into well defined patterns according to the system or combination of systems chiefly involved These patterns include pyrexia of uncertain origin, peripheral neuritis (Kernohan and Woltman 1938) nephritis (Davson Bell and Platt 1948) hypertension bronchial asthma (Harkavy, 1941), obscure abdominal pain (Harris Lynch and O Hara 1939) and myocarditis It is only the last of these with which we are here concerned but when an obscure cardiopathy is accompanied by any of the other manifestations mentioned periarteritis should be seriously considered

Confirmatory evidence includes almost any form of allergic rash visible or palpable nodules along the course of a superficial artery such as the temporal changes in the ocular fundus (including exudates hæmorrhages papillœdema retinal detachment vascular irregularities and occlusion of the central artery of the retina (Sampson 1945)) leucocytosis eosinophilia rapid blood sedimentation rate positive C reactive protein test and *above all a positive muscle or liver biopsy*

*Loffler s syndrome*

Loffler (1932 1936) described a subacute condition of the lungs characterised by transitory infiltrative lesions and eosinophilia This seems to be similar to pulmonary periarteritis as described by Elkeles and Glynn (1944)

*Allergic myocarditis*

Eosinophilic myocarditis as described by Reinhart (1946) and others is also likely to be a variant of polyarteritis

Sulphonamides have been accused of acting as antigens that may provoke allergic myocarditis (French and Weller 1942 French 1946) but a *careful control study by Fawcett (1948) does not support this hypothesis*

*Disseminated lupus*

Disseminated lupus is regarded as a widespread necrosis of connective tissue particularly fibrinoid degeneration of collagen fibres (Klemperer

Pollack and Baehr 1941) resulting from some crucial disturbance of antigen antibody reaction

Like periarteritis it affects chiefly young adults but unlike periarteritis it attacks women in 90 per cent of cases A previous history of lupus erythematosis (butterfly rash) is obtained in at least one third of all cases The illness is apt to be precipitated by some infection drug therapy or physical agent (such as sunburn)

The clinical features include fever patchy erythematous rashes painless erythematous macules (usually in the thenar or hypothenar emminences) tender nodules more deeply situated in the skin (like Osler s nodes) hyperæmia of the nail folds petechiæ or purpura small hæmorrhagic necrotic lesions in the fingers or mouth polyarthritis not unlike that seen in rheumatic fever generalised adenopathy transient infiltrative lesions in the lungs which may cause hæmoptysis vascular lesions in the ocular fundus and cardiac manifestations consisting of pericarditis myocarditis and the verrucous endocarditis of Libman and Sachs (1924) Pericardial effusion may occur (Humphreys 1948) The myocarditis itself behaves functionally like isolated myocarditis Endocarditis when present is apt to affect the tricuspid as well as the mitral or aortic valve The vegetations are larger than in rheumatic valvitis but less damaging than in bacterial endocarditis Histological details have been given by Gross (1940) and the subject has been well reviewed by Griffith and Vural (1951)

The diagnosis of disseminated lupus may be confirmed by leucopenia thrombocytopenia hypochromic anæmia a raised sedimentation rate absence of C reactive protein the presence of cold agglutinins L E cells in the bone marrow and peripheral blood hyperglobulinæmia increased gamma globulin reversal of the albumin/globulin ratio and increased heparin tolerance These tests have been reviewed by Gold and Gowing (1953)

*Scleroderma*

Another collagen disease that may affect the heart is scleroderma Here the connective tissue of the skin, œsophagus joints and heart is chiefly and diffusely involved

The sexes are about equally affected and the average age is nearer 40 than 30

In addition to the smooth shiny fixed skin of the affected areas the majority of cases have Raynaud s syndrome (often the first symptom) polyarthritis (like rheumatoid) and pigmentation of the exposed surfaces of the skin (Weis *et al* 1943) About half the cases have some difficulty in swallowing and reduced peristalsis with delay in the passage of barium through the œsophagus may be demonstrated radiologically (Olsen *et al* 1945) Occasionally the lungs are involved and rarely the kidneys

Many cases of scleroderma heart disease have been reported the majority

proving fatal within a year or two There is an increase of cellular vascular connective tissue with secondary degeneration of muscle fibres followed by replacement fibrosis

There are no specific laboratory tests for scleroderma except the microscopic appearances of biopsied skin Patients are usually afebrile but may have a raised sedimentation rate The C reactive protein test is negative but the serum globulin may be increased For diagnostic purposes clinical hall marks are more helpful

*Dermatomyositis* is similar to scleroderma in most of the above respects but involves muscle as well as skin (Tager and Grossman, 1944)

### *Treatment of myocarditis due to collagen diseases*

Few cases of myocarditis due to any of the collagen diseases or allergic states (except rheumatic carditis) survive more than two years whatever treatment is given A C T H, cortisone, hydrocortisone or preferably one of the newer compounds such as decortisyl (delta 1 dehydrocortisone) that do not cause sodium retention may be tried The usual dose of cortisone in these cases is 200–300 mg daily for the first week 100–150 mg daily for the second, and 50–75 mg daily for the third it is then gradually reduced to the minimum that seems to control the disease A strict low sodium diet and mercurial diuretics help to combat sodium retention The dose of decortisyl is one quarter of the dose of cortisone Withholding the drug all too frequently results in a violent exacerbation of activity and few cases derive much benefit Disseminated lupus responds best (Cohen and Cadman 1953)

### *Sarcoidosis*

The precise nature of sarcoidosis is still uncertain (Scadding 1950) It may affect the cardiovascular system in two ways, both of which are rare extensive pulmonary involvement may cause cor pulmonale (q v ) or there may be an actual sarcoid myocarditis

The clinical features of the cardiopathy resemble those of isolated myocarditis cases may present with congestive failure (Yesner and Silver 1951) or with cardiac pain, suggesting ischæmic heart disease (Stephen 1954), sudden death may occur

The diagnosis may be suggested by coincident pulmonary lesions mediastinal or generalised lymphadenopathy splenomegaly erythema nodosum iridocyclitis and hyperglobulinæmia it may be confirmed by biopsy of an enlarged gland, skin lesion or liver In doubtful cases a saline emulsion of sarcoid tissue may be injected intradermally (Kveim test) the insidious development of a dusky red nodule at the site of injection having the histological appearances of sarcoid is diagnostic (James and Thompson 1955)

## METABOLIC AND NUTRITIONAL CARDIOPATHIES

These include primary amyloidosis hæmochromatosis diabetes mellitus beri beri alcoholism and perhaps endomyocardial fibrosis a congenital group comprising fibroelastosis anomalous origin of the left coronary artery from the pulmonary artery Von Gierke s disease gargoylism and possibly familial cardiomegaly, has already been described in Chapter VIII and is therefore omitted here

### *Primary amyloidosis*

This is a rare metabolic disorder of unknown etiology affecting middle aged or elderly persons of either sex The heart is involved in 85 per cent of cases (Eisen 1946) seriously so in at least 50 per cent (Lindsay 1946) Amyloid material accumulates in the interstitial spaces between secondarily atrophic muscle fibres, and in the walls of the blood vessels (Larsen 1930)

The majority of cases present clinically like isolated myocarditis i e with congestive heart failure of obscure etiology There are very few clues pointing to the true nature of the cardiopathy—only the age of the patient which is usually over 50 (Jones and Frazier 1950) macroglossia and profound asthenia (Eisen 1946) There is of course no history of chronic suppuration or other infection in these primary cases and the congo red test is negative Virtually all laboratory tests selected in the hope of identifying the nature of an obscure cardiopathy are negative except biopsies of the tongue, or possibly skeletal muscle which may reveal amyloid

The two most important diagnostic errors are (1) mistaking amyloid for Pick s disease which may lead to a fruitless and dangerous thoracotomy (Couter and Reichert 1950) and (2) misinterpreting abnormal Q or QS waves and inverted T waves in the electrocardiogram as evidence of cardiac infarction (Wessler and Freedberg 1948 Holzmann 1950) The differential diagnosis between both these conditions and isolated myocarditis has already been discussed

### *Hæmochromatosis*

The disorder of iron metabolism known as hæmochromatosis may affect the heart as well as the pancreas liver, testicles adrenals skin and other organs Althausen and Kerr (1933) emphasised the serious consequences of cardiac involvement and in his classic monograph Sheldon (1935) stated that heart failure was the cause of death in 15 per cent of 119 cases Iron is absorbed avidly from the intestinal tract reaches a relatively high level in the blood is poorly excreted and is deposited in the organs mentioned above Diabetes mellitus muddy pigmentation of the skin loss of axillary and pubic hair testicular atrophy and impotence cirrhosis of the liver and heart failure are the chief consequences Deposition of iron in the muscle fibres of the heart is common in cases without disturbance of

cardiac function (de Gennes *et al*, 1936), but it has usually been more conspicuous in cases of heart failure and secondary fibrosis more evident

Of the 311 cases reviewed by Sheldon (1935) about 95 per cent were men The usual age is between 45 and 60 but cardiac cases tend to be younger all but three out of 25 such cases reviewed by Petit (1945) being under 45

The chief cardiac manifestations are disturbances of rhythm (including heart block and ventricular fibrillation) and heart failure which may be mainly left ventricular or congestive' but pain resembling that in ischæmic heart disease may occur (Horns, 1949) as in isolated myocarditis

The diagnosis is usually obvious owing to the many characteristic features of the disease as a whole, but when the heart bears the brunt of the attack in a young adult it may be overlooked Hæmochromatosis may be proved by biopsy of the skin or liver (King and Downie, 1948) Absorption storage and excretion of iron may be studied by giving radioiron and following its course in the fæces blood and body organs (Bothwell *et al* 1952)

### *Diabetes mellitus*

The relationship between diabetes, blood lipids atherosclerosis peripheral vascular disease and coronary disease is familiar if not fully understood In addition some confusion may be caused by the presence of depressed S T segments or inverted T waves in the electrocardiogram in patients without other evidence of coronary disease these appearances have been attributed to a low blood potassium following treatment for diabetic acidosis (Liebow and Hellerstein 1949 Henderson 1953) too much insulin therapy may also precipitate or aggravate latent angina pectoris for hypoglycæmia causes hyperadrenalism and this too may alter the electrocardiogram Finally, circulatory collapse in diabetic coma may temporarily impair the nutrition of the myocardium Apart from these considerations diabetes mellitus does not injure the heart

### *The heart in malnutrition and chronic alcoholism*

The heart may be seriously affected by nutritional anæmia and beri beri, both conditions give rise to a hyperkinetic circulatory state and are discussed under that heading The term *nutritional cardiopathy* is best reserved for that form of heart disease that may result from an unbalanced high carbohydrate low protein diet as described by Gillanders (1951). The disorder is common amongst the adult Bantu population of South Africa and something very similar may be seen in chronic alcoholics anywhere At necropsy the heart is dilated and hypertrophied and microscopy shows hypertrophy of the muscle fibres without loss of striation or hydropic degeneration intracellular œdema may occur but is not specific being found in many types of heart failure patchy interstitial fibrosis is also described but may be inconspicuous There are no inflammatory foci and

the endocardium is normal except where it underlies organised mural thrombi which are common in both ventricles and atria In other words the findings are simply those of chronic heart failure without demonstrable cause (Higginson Gillanders and Murray 1952) Varying degrees of cirrhosis of the liver thought to be due to the same malnutrition are found in nearly all cases heavy deposits of hæmosiderin are common in the liver and other abdominal organs but not in the heart itself

The post mortem findings in chronic alcoholics dying from heart failure are similar although the intracellular œdema has been specially emphasised (Merle and Belin 1953) The hepatic hypoprotinæmic metabolic cardiopathy described by Oppenheim (1950) in cases of cirrhosis of the liver may be similar but may also include hepatic hyperkinetic circulatory states

*Clinically* cases present with the characteristic dietetic or alcoholic history and congestive heart failure with a low cardiac output Atrial flutter is particularly common in alcoholic cases

The *differential diagnosis* is from beri beri hæmochromatosis and hepatic cardiopathy Beri beri is excluded by the low cardiac output absence of response to aneurin and negative biochemical and biological tests for aneurin deficiency Cases may occur however in which B1 deficiency is also present and therapeutically it is wise to cover the possibility Hæmosiderosis may be found in hepatic biopsies and is believed to be another result of chronic malnutrition (Gillman and Gillman 1951) hæmochromatosis involving the heart is unlikely in the absence of any other evidence of that disease Associated cirrhosis of the liver may be advanced especially in chronic alcoholics and may lead to vasodilatation and an attempt to raise the cardiac output The combination of nutritional and hepatic cardiopathies may be confusing and may result in an erroneous diagnosis of beri beri but the hepatic palms spider nævi small volume collapsing pulse low blood pressure and absence of response to thiamine should soon correct the mistake

Treatment consists of a high protein well balanced diet which if given in time may reverse the myocardial fault Too often however it is already too late or the diet is not maintained The usual remedies for heart failure must also be prescribed

## ENDOCRINE CARDIOPATHIES

*Thyrotoxicosis and myxœdema* are by far the most important endocrine diseases that affect the cardiovascular system They are discussed separately in Chapter XIX

*Acromegaly* may cause considerable cardiac hypertrophy and hyperplasia of interstitial fibrous tissue Enlargement of other viscera usually accompanies the cardiomegaly Many hearts from acromegalics have weighed over 1 000 G (Courville and Mason 1938) Hypertension and coronary disease associated with diabetes complicate some of the cases but

heart failure may occur in their absence (Hejtmancik Bradfield and Herrman, 1951) Failure is attributed to enlargement outstripping nutritional supplies

## NEUROMUSCULAR DYSTROPHIES

*Friedreich s ataxia* has been discussed in the congenital section

*Progressive muscular dystrophy* involves the heart in about 50 per cent of cases (Rubin and Buchberg 1952) There is muscular atrophy and fibrous tissue replacement (Weisenfeld and Messinger 1952) There seems to be little relationship between the degree and severity of the skeletal myopathy and the cardiac lesion

The great majority of cases are male and the average age 25 (Zatuch *et al* 1951)

Clinically the most common finding is some abnormality in the electrocardiogram such as bundle branch block or T wave changes without serious disturbance of cardiac function Arrhythmias also occur, and in a minority congestive heart failure Sudden death has been reported in several instances

The diagnosis should be suggested by the prominent yet weak calf muscles the awkward gait and the habit of climbing up the legs when getting up it may be proved by muscle biopsy

## TUMOURS OF THE HEART

Primary tumours are rare and include myxoma (35 per cent) sarcoma (21 per cent) fibroma (12 per cent) rhabdomyoma (19 per cent) and lipoma (12 per cent) (Yater 1931) Secondary tumours are sixteen times more common (Reeves and Michael, 1936) they have been found at necropsy in 10 per cent of all cases of malignant disease but have given rise to clinical manifestations in only 1 per cent (Goudie 1955) The majority are secondary to carcinoma of the bronchus or breast but almost any malignant tumour may metastasise to the heart (Raven 1948 Young and Goldman 1954) Leukæmia must also be considered in this section

MYXOMA OF THE LEFT ATRIUM is the commonest primary tumour of the heart It arises from the atrial septum to which it is attached by a pedicle close to the foramen ovale

The majority of patients have been women between the ages of 30 and 60

Symptoms may develop relatively suddenly and are attributable to acute subacute chronic or paroxysmal obstruction at the mitral orifice Severe syncopal attacks during which the pulse may be imperceptible acute pulmonary œdema or paroxysmal nocturnal dyspnœa may occur A chronic course ending in congestive heart failure has also been described Arrhythmias are said to be infrequent but paroxysmal atrial tachycardia and atrial fibrillation have both been recorded (Gilchrist and Miller 1936 Fawcett and Ward 1939)

The physical signs include a small peripheral pulse and remarkably variable mitral systolic and diastolic murmurs In some cases however no murmurs are heard at all (Von Reis 1949) The records in the literature rarely mention the first heart sound or the presence or absence of a mitral opening snap but Burnett and Davidson (1945) stated that the first heart sound was accentuated in their case as did Jones and Julian (1955) and all observers have likened the signs to those of variable mitral stenosis with or without pulmonary hypertension (Mahaim 1947) The P wave of the electrocardiogram has usually been more or less normal and as a rule X rays have revealed little enlargement of the left atrium and pulmonary artery Few illustrations of chronic pulmonary interstitial œdema have been published

The physiological findings on cardiac catheterisation may prove as variable as the murmurs and this itself may suggest the correct diagnosis myxoma should al o be suspected if the left atrial pressure is found to be normal in a case of supposed mitral stenosis giving a history of paroxysmal cardiac dyspnœa Angiocardiography may reveal a filling defect of the left atrium (Goldberg and Steinberg 1955)

In the case reported by Jones and Julian (1955) the mean left atrial pressure was 44 mm Hg and the mean pulmonary artery pressure 80 mm Hg Left atrial pressures as high as this at rest are very unusual in mitral stenosis particularly in cases with so short a history Even passive pulmonary hypertension of this degree could well cause right ventricular failure

The downhill course is usually rapid few patients surviving more than a year after the onset of symptoms Death may terminate a syncopal attack or result from acute pulmonary œdema

*Treatment* is surgical In cases of acute pulmonary œdema or loss of consciousness it is worth changing the position of the patient in the hope that the tumour may slip away from the mitral orifice

PRIMARY SARCOMA of the heart arises from the right atrium in at least half the cases (Weir and Jones 1941) and as it grows tends to fill the cavities of both the right atrium and right ventricle Hæmangioendothelio arcoma behaves similarly (Cheng and Sutton 1955 Amsterdam *et al* 1949) These tumours may be highly vascular and are composed chiefly of nests of hæmangioblasts in a groundwork of endothelial cells

The clinical features of sarcoma of the right atrium closely resemble those of rapidly progressive tricuspid stenosis the obstruction of the circulation being more or less at the level of the tricuspid valve through which the tumour usually grows

FIBROMA is most likely to involve the wall of the left ventricle The only example I have seen was in a female child who presented with paroxysmal ventricular tachycardia heart failure which finally proved fatal an electro cardiogram with a QT pattern suggesting cardiac infarction in anterolateral



Fig 11 05—Fibroma of the left ventricle
(*Ack l dgm t t D U la Jame* )

left ventricular surface leads or their equivalents and radiological appearances resembling a large left ventricular aneurysm (fig 11 05)

RHABDOMYOMA is a congenital glycogen containing tumour of heart muscle fibres (ῥάβδος a rod) and is more often multiple than solitary The nodules are usually found in the wall of the left ventricle and may be associated with tuberose sclerosis Most cases die in infancy or childhood (Batchelor and Maun 1945)

SECONDARY TUMOURS involve the heart or pericardium in about 10 per cent of all cases of cancer (Scott and Garvin 1939) The majority are secondary to bronchial carcinoma and invade the heart by direct extension the pericardium being affected first Thymic and other mediastinal neo plasms may spread to the heart in the same way

Clinically such cases tend to present with hæmopericardium often with cardiac tamponade in others paroxysmal atrial tachycardia or flutter is the first manifestation Sometimes pericardial pain and inverted T waves in the electrocardiogram are mistaken for cardiac infarction especially when followed by intractable heart failure

Discrete blood born secondary nodules from remote malignant growths are less frequent and when present may be associated with more obvious secondaries in the lungs

LEUKÆMIA may give rise to infiltrative myocardial or pericardial lesions but they are rarely of much clinical importance Associated severe anæmia is more likely to embarrass the cardiovascular system I have only seen five cases of leukæmia amongst my last 10 000 patients with cardiovascular disease three of these presented with acute cardiac infarction from coronary thrombosis one with acute coronary insufficiency after a long history of angina pectoris and one with a hyperkinetic circulatory state due to severe anæmia The patients with occlusive coronary disease were all elderly men and the leukæmia was discovered as a result of a routine white count Whether the two diseases were coincidental or related is unknown The leukæmia was monocytic in three cases and myeloid in the other two

*Argentaffinoma*

In 1952 Biorck Axen and Thorson described the unusual association of pulmonary valve stenosis gross tricuspid incompetence and carcinoid of the small intestine with metastases in the liver in a boy of 19, a remarkable feature of the case was intense patchy and variable reddish blue cyanosis and attacks of flushing there was also a nine year history of asthma and diarrhoea In 1954 Thorson Biorck and Bjorkman reported seven definite cases of this interesting syndrome and concluded that the secretion of large quantities of serotonin (5 hydroxytryptamine) by the carcinoid and its metastases was responsible for the acquired pulmonary and tricuspid valve lesions as well as for flushing patchy cyanosis bronchospasm and diarrhoea The syndrome has excited considerable interest and a number of similar cases have been reported by others since (e g Bean *et al*, 1955)

*Biochemically* serotonin (5 hydroxytryptamine) has been demonstrated in high concentration in the serum and urine of patients with argentaffinoma of the small intestine (Pernow and Waldenstrom 1954) as well as in the tumour itself and its metastases (Lembeck 1953) Serotonin is inactivated by a lung enzyme—monoamine oxidase (Bradley *et al*, 1950)—which breaks it down to 5 hydroxyindoleacetic acid (5 H I A A ) and an enormous increase of this substance has been found in the urine of patients with argentaffinoma (Page *et al* 1955) In a case of my own there was good evidence that serotonin was inactivated in the lungs because its concentration in the serum and plasma fell from 56 and 62 $\mu$g per cent respectively in samples from the pulmonary artery to 19 and 22 $\mu$g per cent respectively in samples obtained from the brachial artery (Goble Hay and Sandler 1955) It is not yet clear how serotonin causes fusion of the pulmonary and tricuspid valve cusps, but its inactivation in the lung explains why the valve lesions are right sided

*Clinically* the syndrome is easily recognised by anyone familiar with its manifestations The combination of the peculiar mottled or patchy cyanosis the attacks of flushing and bronchial asthma the diarrhoea large liver (from metastases) and signs of mild or moderate pulmonary and tricuspid stenosis are too characteristic to be mistaken for any other condition In my own case (a 33 year old woman) the pulmonary stenosis was of moderate degree (P A P 9/4 R V P 45/-5 C O 3 5 L/min at rest) and the tricuspid stenosis mild (presystolic pressure gradient 4 mm Hg) There was a two year history of blotchy erythema marked flushing and asthma attacks being precipitated by meals so that she became afraid to eat The primary tumour was removed from the ileum but there was little improvement owing to the extensive metastases in the liver and she died within six months of her first admission to hospital Necropsy confirmed the diagnosis Full details of this case are being reported by Goble *et al* (1956)

## MYOCARDITIS DUE TO DRUGS

Certain therapeutic drugs have earned the reputation of being dangerous to the heart either by causing transient toxic myocarditis or by inducing ventricular fibrillation or asystole In the first group the best known are digitalis and emetine in the second choloroform adrenaline and potassium Toxic myocarditis due to drug allergy is in a different category and has already been discussed

### *DIGITALIS*

Digitalis is undoubtedly the best example of a therapeutic drug that may cause dangerous myocardial poisoning

*Pathology* Buchner (1934) first demonstrated that necrotic myocardial lesions could be produced in animals (cats) by means of digitalis Dearing Barnes and Essex (1943) also working on cats produced focal necrosis cellular reaction and fibroblastic repair Similar necrotic lesions may be provoked by acetylcholine and by continuous direct vagal stimulation (Banting and Hall 1936 1937) and have been ascribed to coronary constriction In the belief that the lesions due to digitalis were caused by the activity of acetylcholine Kyser Ginsberg and Gilbert (1946) succeeded in

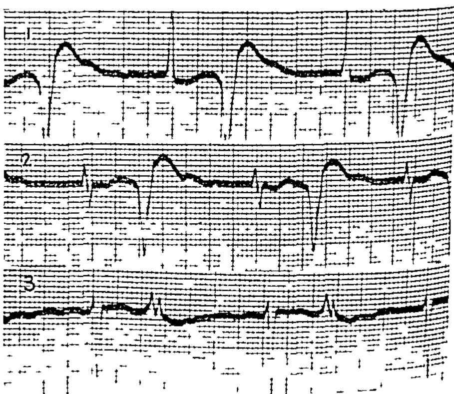



Fig 11 06—Electrocardiogram showing coupling from ventricular ectopic beats due to digitalis

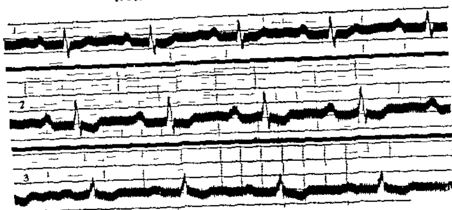



Fig 11 07—Electrocardiogram showing partial heart block due to digitalis

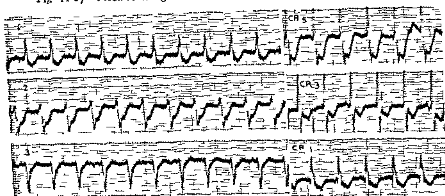



Fig 11 08—Electrocardiogram showing paroxysmal tachycardia due to digitalis

preventing them by the simultaneous administration of atropine or a coronary vasodilator such as theophylline Whether digitalis intoxication in man is characterised by similar patchy myocardial necrosis and whether this is mediated by vagal stimulation remain to be proved but it is a reasonable hypothesis Certainly the effect of acetylcholine is augmented in the presence of strophanthin or digitalis (Danielopolu 1946)

*Clinical features* Anorexia nausea or vomiting and diarrhœa usually give sufficient warning of digitalis overdosage but there may be no such indication when carditis from other causes is already present Disturbances of rhythm are common and include coupling due to premature ectopic beats (fig 11 06) nodal rhythm partial or complete heart block (fig 11 07) multiple ectopic beats atrial fibrillation paroxysmal tachycardia (fig 11 08) and sudden death from ventricular fibrillation

The electrocardiogram shows characteristic sagging depression of the RS T segment (fig 11 09) maximum in leads $V_{4-6}$ when there is normal or increased left ventricular dominance or in leads $V_1$ when there is right ventricular preponderance The depression is transmitted chiefly to

lead $V_L$ or $V_F$ and thence to the appropriate standard lead according to the electrical position of the heart At first the peak of T remains upright but later becomes absorbed in a sharply depressed RS T segment, the Q T interval being shortened (fig 11 10) The electrocardiogram offers by far the most reliable evidence of digitalis saturation even when the patient denies having taken the drug

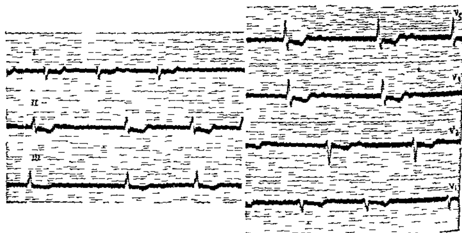



Fig 11 09—Electrocardiogram showing depression of the RS T segment due to digitalis

Fig 11 10—Shortening of the Q T interval due to digitalis Q Tc—0 3 sec

*Treatment* The best remedy apart from stopping digitalis is atropine but it is rarely necessary If the degree of intoxication appears dangerous however it may be given in doses of 0 5 mg four hourly for a day or two

## EMETINE

Emetine is another therapeutic drug with a reputation for causing toxic myocarditis the chief danger being abnormalities of rhythm particularly ventricular fibrillation Emetine was used a great deal amongst British troops in the Mediterranean theatre during the second world war but ill effects on the heart were very rare if they occurred at all Patients receiving emetine however were always confined to bed throughout the course

Fatal cases of toxic myocarditis described in the literature received a total dose of 1 04 to 2 65 G of emetine over a period of two to six weeks (Brown 1935) Emetine is highly cumulative being excreted very slowly and the minimum lethal dose is said to be around 20 mg /kilo

## OTHER DRUGS

*Potassium* when used in large single doses (8 to 16 G ) to stop paroxysmal tachycardia or multiple ectopic beats or to differentiate between ischæmic and other causes of T wave inversion is undoubtedly dangerous and may cause sudden death from ventricular asystole preceded by increasing heart block and bundle branch block Spontaneous potassium poisoning may cause sudden death in uræmia (Marchand and Finch 1944) The electro cardiogram in such cases shows widened QRS complexes and tall peaked T waves (fig 11 11)

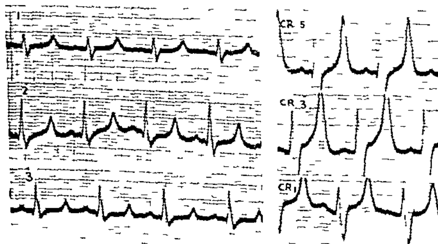



Fig 11 11—Widening of the QRS complex and accentuation of the T wave due to a high blood potassium in a case of uræmia The long Q T is due to hypocalcæmia

The normal serum potassium is 15 to 21 mg per cent (4 to 5.5 m eq per litre) It may be reduced in a variety of conditions including familial periodic paralysis diabetic acidosis ulcerative colitis idiopathic steatorrhœa, vomiting from interstinal obstruction and as a result of prolonged treatment with resins Electrocardiographic changes include flattening of the T wave, augmentation of the U wave, depression of the S T segment and prolongation of the P R Q T and Q U intervals (Perelson and Cosby 1949 Bellet *et al* 1950) The amplitude of T declines when the serum potassium is at 13 to 14 mg per cent U becomes prominent at 10 to 12 mg per cent and depression of the S T segment at about 8 mg per cent (Metzger and Blum 1950) Ectopic beats and perhaps other arrhythmias may result from these low potassium levels and McAllen (1955) found widespread myocardial fibrosis at necropsy in two cases

*Adrenaline* in large doses may excite ectopic beats or almost any change of rhythm except heart block Transient hypertension and inversion of the T wave in leads $V_{4-6}$ are common Violent palpitations and substernal discomfort may occur and patients with ischæmic heart disease usually develop a severe attack of angina pectoris Clinical examples may result from errors in the dose of adrenaline administered or from spontaneous hyperadrenalism in cases of pheochromocytoma

*Chloroform* is an example of a group of drugs mostly anæsthetics which may cause sudden death from ventricular fibrillation especially in the presence of an excess of adrenaline

*Nicotine* as absorbed by heavy smokers may provoke ectopic beats and cause slight coronary and peripheral vasoconstriction and so aggravate angina pectoris hypertension and peripheral vascular disease *Barium chloride* causes ectopic beats

*Alcohol* is a vasodilator and in moderate amounts may benefit ischæmic heart disease on the other hand it may increase the work of the heart especially if the blood volume is temporarily raised Heavy drinkers may suffer from an inadequate supply of aneurin and may develop heart failure in consequence or their high carbohydrate low protein diet may lead to another form of nutritional cardiopathy as described on page 658 Finally under the influence of alcohol patients are apt to be careless of medical advice and may exert themselves more than they should

## THE HEART IN ACUTE NEPHRITIS

Carditis accompanying acute nephritis (Whitehill *et al* 1939) and toxæmia of pregnancy (Szekely and Snaith 1947) is particularly interesting The chief clinical features are elevation of the venous pressure a tendency to develop acute pulmonary œdema general enlargement of the heart and inversion of the T wave in leads facing the surface of the left ventricle (Master Jaffe and Dack 1937) The degree of hypertension is often insufficient to explain these findings Nephritic œdema is usually present the blood volume is raised and the circulation time normal (Klein 1947)

That there may be some form of cardiopathy is suggested in certain cases by the behaviour of the cardiac output which may fail to rise as expected when the venous pressure is high moreover the Valsalva test yields a square wave response (Sharpey Schafer 1955) On the other hand

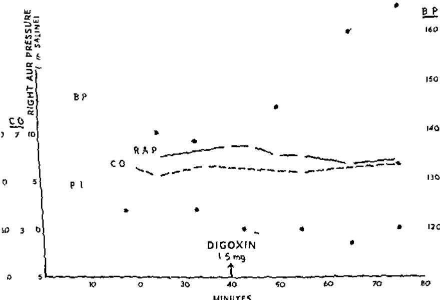



Fig 11 12—Graph illustrating a high right atrial pressure that is not reduced by digitalis in a case of acute nephritis There is a conspicuous rise of blood pressure and slight slowing of the pulse the cardiac output is unchanged

the lack of response to digitalis (fig 11 12) shows that the heart is not over loaded Histological examination of the heart muscle in fatal cases of acute nephritis presenting cardiac signs seldom reveals any structural abnormality sometimes however the muscle fibres are dispersed by serous exudate lymphocytes and endothelial cells—even then there is little if any necrosis (Gore and Saphir 1948)

It is probable therefore that the raised venous pressure is mainly due to an increased blood volume from retention of sodium and water, and that as a rule the heart responds normally but that in certain instances cardiac function is impaired owing perhaps to biochemical rather than structural changes in the heart muscle, whether acute pulmonary œdema is a manifestation of left ventricular failure or whether it is due to a toxic or allergic effect on the pulmonary capillaries is not yet known

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# BACTERIAL ENDOCARDITIS

BACTERIAL or infective endocarditis means bacterial infection of any of the heart valves or of certain congenital anomalies of the heart or great vessels (bacterial endarteritis) It occurs in two main forms acute (malignant), due to infection with any of the pyogenic bacteria and subacute, due mainly to the *Streptococcus viridans* but many other organisms have been isolated from both types This broad classification is necessarily artificial, the course of the disease depending on the virulence of the organism and the resistance of the host There is no clear division between the two types and they are better considered as one disease

There is usually some underlying fault congenital (10 per cent) or acquired The most susceptible congenital anomalies are pulmonary stenosis bicuspid aortic valve ventricular septal defect and patent ductus arteriosus atrial septal defect is remarkably immune Any acquired valve lesion may become infected including syphilitic aortic incompetence (Martin and Adams 1938) and calcific aortic stenosis (Brink and Smith 1937) but old rheumatic valvulitis is to blame in 80 per cent of cases (Clawson 1948) In quite a number active rheumatic infection is still present when bacterial endocarditis is superimposed The most susceptible valve fault is mild mitral incompetence

## PATHOLOGY

The lesion is superficial and is not a valvulitis in the sense that rheumatic endocarditis is bacteria invade the surface of a damaged or congenitally deformed valve and are encouraged by the formation of small superficial thrombi which provide an excellent culture medium Both in the natural disease and experimentally in dogs there appears to be a paucity of granulation tissue and of cellular reaction the microbes are not destroyed and healing does not take place Elsewhere in the body similar foci of bacteria are rapidly walled off by granulation tissue and the lesion is invaded by leucocytes the microbes are destroyed and the inflammation soon subside (Friedman Katz Howell *et al* 1938)

The macroscopic appearances vary according to the infecting organism, tending to be finely granular with streptococcus viridans ulcerative and hæmorrhagic with the hæmolytic streptococcus and pneumococcus proliferative with the gonococcus When associated with congenital defects the site of the vegetations depends upon the direction of blood flow through the defect thus in the maladie de Roger vegetations are found on the right side of the patent interventricular septum and on the wall of the right

ventricle opposite the defect with patent ductus arteriosus they are found at the pulmonary artery end Ulceration may lead to perforation of a valve cusp or sinus of Valsalva In old rheumatic cases vegetations may spread on to the endocardium of the left atrium (Thayer 1926)

The myocardium may show scattered focal lesions similar to those seen in isolated or toxic myocarditis or small collections of lymphocytes or lymphocytes and polymorphs known as Bracht Wachter bodies (Bracht and Wachter 1909) The latter are believed to be embolic in origin and represent a local inflammatory reaction to bacterial nests (Perry 1936) They are the non suppurative counterpart of the miliary abscesses seen in staphylococcal cases Saphir Katz and Gore (1950) found myocardial lesions in all of 76 fatal cases they included emboli micro infarcts peri vascular infiltration micro abscesses interstitial infiltration and myo cardial necrosis

## OCCURRENCE

Bacterial endocarditis accounts for about 2 per cent of all cases of organic heart disease (White 1937) and for 9 per cent of all deaths from heart disease (Clawson 1948) It may occur at any age but is most common in young adults of either sex Auricular fibrillation occurs in only 2 5 per cent of cases (McDonald 1946) presumably because it is not a feature of the congenital lesions mentioned is uncommon in rheumatic aortic valve disease and occurs late in the life history of patients with mitral stenosis There is no evidence that the two conditions are mutually antagonistic

## CLINICAL FEATURES

Patients may present themselves with cardiac symptoms pyrexia of un known origin anaemia a cerebral vascular lesion subacute rheumatism nephritis broncho pneumonia or with other patterns which depend upon the nature of the invading organism the underlying cardiac lesion and the caprice of the disease process At the onset symptoms are often ascribed to influenza but fail to clear up A history of dental sepsis or recent tooth extraction is obtained in 48 per cent of cases (Gates and Christie 1951) The diagnosis rests upon the combination of a variety of signs which will be considered individually

*Cardiac abnormalities* There should be evidence of one or other of the various underlying valve lesions or congenital defects already mentioned especially mitral or aortic incompetence and if there are no abnormal auscultatory signs of heart disease the diagnosis is rarely tenable The development of a new valve lesion or of the whining diastolic murmur and thrill of a perforated aortic cusp may be highly suggestive

Toxic myocarditis is not uncommon and may cause heart failure and death whether the infection yields to treatment or not Its importance has been more widely recognised since the introduction of penicillin (Saphir

Katz and Gore 1950) Heart failure occurs most frequently towards the end of the course of antibiotic treatment or during convalescence and was detected in no less than 63 per cent of the 442 cases analysed by Cates and Christie (1951)

*Pyrexia* Acute cases are always febrile subacute cases are always febrile at some stage in the disease but bouts of fever may alternate with afebrile periods The fever is irregular in type usually low grade or moderate in degree and may continue for weeks months or years

*Anæmia* Anæmia nearly always develops early and is already present in about three quarters of the patients when first seen It is indeterminate in type being normocytic and orthochromic, even when associated with hæmolytic infections The red cells may be reduced to about three million and the hæmoglobin to about 60 per cent, giving a normal colour index Stained films and bone marrow samples reveal no specific features If microcytic hypochromic anæmia is found the diagnosis should be doubted for iron deficiency anæmia itself may cause many of the signs and symptoms of bacterial endocarditis e g functional systolic murmurs at the base or the apex of the heart splenomegaly petechiæ red cells in the urine, and even low grade pyrexia

The white count is variable It may be normal on the other hand there may be moderate leucocytosis or leucopenia Leucocytosis is usually associated with acute septicæmic cases normal or leucopenic counts with subacute infections

*Splenomegaly* The spleen is usually palpable It may be soft as in typhoid when due to septicæmia it may enlarge rather suddenly as a result of splenic infarction when it is tender it may be firm in subacute cases or it may be so large as to cross the mid line in chronic cases

*Petechiæ* Petechiæ are common and sometimes appear in successive crops They may be seen under the nails in the ocular fundi in the conjunctivæ or anywhere in the skin or mucous membranes Under the nails they resemble small splinters (Horder 1926) in the fundi they may have white centres of exudate in the skin they must be distinguished from minute telangiectases—Campbell de Morgan s spots Petechiæ in successive crops or otherwise are in no way diagnostic of bacterial endocarditis They are due to capillary hæmorrhage and may occur in any condition in which the capillaries are suitably damaged including most forms of septicæmia acute rheumatic fever (especially when associated with acute glomerulonephritis) and severe anæmia In bacterial endocarditis the capillary lesion may be due to toxins, to allergy or to anæmia

Increased capillary fragility may be demonstrated by the capillary resistance test

A cuff is placed on the upper arm inflated to a pressure of 50 mm. of mercury and maintained for five minutes alternatively a pressure of 80 mm of mercury may be maintained for three minutes The arm below the cuff is then inspected. Most normal subjects are unaffected but some develop a few tiny petechiæ in the

ante cubital fossa The result of the test may be expressed as slightly moderately considerably or grossly positive or as negative the four positive grades representing transitions from a few tiny hæmorrhages to gross purpura

The test may be positive or negative in bacterial endocarditis when spontaneous petechiæ are present When positive it is well to make sure that vitamin deficiency is not responsible or to cover this possibility by giving adequate doses of ascorbic acid rutin and crude vitamin P

Small hæmorrhagic pustules in the skin may occur in the acute pyogenic forms of bacterial endocarditis and are embolic in origin

*Clubbing of the fingers (and toes)* Clubbing occurs in about half of the subacute cases but as it takes at least 3 to 6 weeks to develop it is rare in malignant endocarditis Early clubbing may be recognised by noting congestion and thickening of the nail fold and loss of the normal angulation between the nail fold and the base of the nail Slight clubbing should be interpreted with caution however for it may occur in many conditions including active rheumatic carditis Conspicuous clubbing on the other hand provides excellent supportive evidence of bacterial endocarditis if cyanotic congenital heart disease pulmonary abscess bronchogenic carcinoma and a congenital origin can be excluded

*Nodes* Osler s nodes are small transient erythematous lesions about the size of a pea lasting a few days and vivid pink in colour when fresh bluish when fading often with a darker centre they are raised palpable and tender and may be found particularly on the pads of the fingers and toes on the sides of the fingers or on the thenar or hypothenar eminences (Osler 1909) They are due to infected cutaneous emboli and the responsible organism may sometimes be cultured from them

More important perhaps because more common are larger deeper nodes which vary from the size of a pea to that of a grapefruit They are red painful hot and tender, may occur anywhere in the limbs and may be mistaken for osteomyelitis or periostitis When a lesion involves the finger it closely resembles an ordinary infected pulp it is non suppurative however and disappears in about a week if left alone Cultures from the inflamed tissue may yield *Streptococcus viridans* Red tender macules are equally characteristic and even more common and may also yield positive cultures from biopsies

*Emboli* In addition to the minute emboli which cause white centred petechiæ and the nodes just mentioned larger emboli may block any artery —cerebral, visceral, or peripheral They are more common in the radial ulner, posterior tibial and dorsal artery of the foot than in the axillary or femoral artery because their size is limited For this reason peripheral emboli are often symptomless and are only discovered by those who look for them In cases of suspected bacterial endocarditis the peripheral vessels should always be palpated and their patency noted for future reference In the series of 442 cases reported by Cates and Christie (1951) a major arterial embolism occurred in 35 per cent

*Mycotic aneurysm* Ulceration or degeneration of the wall of an artery due to local inflammation from an infected embolus lodging within the vessel or in its vasa vasorum may result in the formation of a small aneurysm. Severe hæmorrhage results from rupture of a mycotic aneurysm and may prove fatal if cerebral or visceral

*Pulmonary emboli* When bacterial endocarditis involves the pulmonary or tricuspid valve or when it is associated with a left to right cardiac shunt as in patent interventricular septum emboli may be flung into the pulmonary circulation Numerous small pulmonary infarcts result and may give rise to a clinical picture resembling recurrent or subacute hæmorrhagic bronchopneumonia

*Renal lesions* The various renal lesions that may occur in bacterial endocarditis represent almost every aspect of the disease

(1) An embolus lodging in a small renal artery leads to simple infarction of the kidney with hæmaturia or without signs or symptoms

(2) Minute bacterial emboli may cause embolic nephritis which in greater or less degree is found in the majority of cases Only some of the glomeruli are involved rarely more than 60 per cent and most of these have some of their capillary loops intact so that the tuft is not entirely avascular and the health of the tubules is not seriously threatened Affected capillaries are converted into a hyaline mass and red cells may be found in the capsular space and in the urine Embolic nephritis does not cause renal failure because a sufficient number of glomeruli are always spared (Baehr 1921)

(3) In acute pyogenic forms of bacterial endocarditis particularly when pneumococcal or staphylococcal in origin miliary abscesses may be found in the substance of the kidney

(4) Petechiæ due to simple capillary hæmorrhage may occur on the surface of the kidney in the absence of embolic nephritis They are then similar to those found in the pericardium pleura and skin

(5) Acute diffuse glomerulo nephritis may occur as with other streptococcal infections and may progress to renal failure but not more than 5 to 10 per cent of all cases take this course

(6) Simple congestion of the kidney may result from heart failure and give rise to albuminuria and to a few red cells in the urine

It will be appreciated that these six types of renal lesion represent thrombotic emboli benign bacterial emboli septic emboli simple hæmorrhage toxæmia or allergy and heart failure respectively, and that nearly all the features of bacterial endocarditis may be understood in terms of these six factors

*Changes in the ocular fundus* Simple petechiæ like those in the skin are fairly common Occasionally they have white centres and may be embolic in origin It should be understood that these white centres represent exu

date and that identical lesions may be seen in other conditions particularly leukæmia and malignant hypertension The exudate may be surrounded by hæmorrhage or may be to one side of it Embolism of the central artery of the retina or of one of its main branches may cause complete or partial loss of vision but is fortunately rare Finally papillædema or papillitis with or without widespread hæmorrhages and exudates is not uncommon when there is diffuse glomerulo nephritis the appearances resembling those of malignant hypertension

## DIAGNOSIS

It is emphasised that pyrexia anæmia splenomegaly petechiæ and diffuse glomerulo nephritis may occur wherever the site of the cardiac lesion that systemic emboli mycotic aneurysms nodes and embolic nephritis signify left sided lesions e g aortic or mitral valve disease that multiple hæmorrhagic infarcts in the lungs are the prerogative of right sided valve lesions and of left to right congenital shunts such as patent ductus and maladie de Roger (Barker 1949)

Clinically bacterial endocarditis should be considered in all cases of unexplained fever with suspicious auscultatory signs in the heart If an indeterminate anæmia is also present a determined search should be made for other evidence if splenomegaly petechiæ and red cells in the urine are added the diagnosis becomes probable but is still uncertain On the other hand clubbing of the fingers nodes peripheral emboli mycotic aneurysm nephritis and characteristic fundal changes may each one of them be diagnostic of bacterial endocarditis when associated with fever and an appropriate cardiac lesion

The diagnosis is confirmed by a positive blood or bone marrow culture Six tubes are usually set up from each sample and 4 to 6 samples should be obtained at different times preferably when the temperature is high before a negative result is accepted It should be pointed out however that blood cultures from patients with pyorrhœa or with dental abscess may grow *Streptococcus viridans* when the specimen is obtained after chewing so that the diagnosis of bacterial endocarditis should never rest on a positive blood culture alone

## NATURAL COURSE

Untreated patients with acute infection die in a matter of days or weeks usually from septicæmia or from the effects of embolism those with sub acute infection usually live for months and occasionally for years bouts of fever with exacerbation of signs and symptoms alternating with afebrile quiescent phases described by Libman as bacteria free periods Death may result from heart failure cerebral or other visceral embolism hæmorrhage uræmia or other causes According to Libman and Friedberg (1941) about 3 per cent of all patients recover spontaneously but Lichtman (1943) found that only 1 per cent of 2 596 cases collected from the literature so recovered

## PROGNOSIS

Penicillin and streptomycin have radically altered the course of bacterial endocarditis for the infection can now be controlled in 90 per cent of cases However about 25 per cent still die during or shortly after treatment mostly from heart failure This high mortality may be due to the frequency of serious toxic myocarditis and to the relatively rapid increase in severity of valve lesions particularly aortic or mitral incompetence Uræmia accounted for only 6 per cent of the 131 deaths in the combined hospitals series reported by Christie (1948) emboli for 11 per cent and hæmorrhage for 8 per cent The most important factors influencing the mortality rate proved to be the presence and degree of heart failure the duration of the infection and the nutritional state of the patient

Relapses are common in inadequately treated cases, but should not exceed 10 per cent in patients who have received at least 0 5 mega unit of penicillin daily for a minimum period of 28 days Nearly all those who relapse do so within one month of ceasing treatment The frequency of recurrence (as distinct from relapse) is not yet known

## TREATMENT

*Prophylactic* Surgical repair of patent ductus arteriosus not only cures the defect but protects the patient from infective endarteritis Repair of coarctation of the aorta may be less successful in the second respect because infection may yet complicate an associated bicuspid aortic valve It is not expected that surgical relief of pulmonary stenosis will reduce the frequency of bacterial endocarditis in that disease

Dental hygiene is particularly important in all patients who have congenital heart disease or chronic valve disease Tooth extractions tonsillectomy and other E N T operations should be covered by 300 000 units of procaine penicillin twice daily for five days or perhaps 600 000 units daily A single intramuscular injection of benzathene penicillin 600 000 units the day before tooth extraction may also suffice but awaits longer trial

*Chemotherapy* Sulphonamides have proved disappointing and although they may temporarily sterilise the blood stream and lower the temperature they rarely cure the disease Of 489 cases treated with sulphonamides alone, only 4 per cent recovered (Lichtman 1943)

The situation has greatly improved since the introduction of penicillin Patients should be treated early as soon as the diagnosis is clinically probable without waiting for positive results of blood cultures Every effort should be made to counter malnutrition and a blood transfusion should be given if there is serious anæmia

The minimum dose of penicillin is 0 5 mega unit daily given in divided doses of 60 000 units three hourly 80 000 units four hourly or 120 000 units six hourly and continued for twenty eight days Nothing less than

this will suffice and larger doses averaging 2 mega daily, prolonged for six to eight weeks are preferred (Cates and Christie 1951) One of my patients was not controlled until she received a million units three hourly and a total of 250 million units If the resistance of the organism is known so much the better but even then the optimum dose cannot be calculated exactly because it depends partly on the physical properties of the lesion Swift and maintained clinical response is the only reliable criterion by which to judge the correct dose If however the resistance of the organism is known to be more than eight times that of the standard test strain of Oxford staphylococcus the dose of penicillin should certainly be increased proportionately (Christie 1948) If the coefficient of resistance is 10 not less than 100 000 units three hourly will suffice if 20 then at least 200 000 units three hourly will be necessary—and so on (Baehr and Gerber, 1947) Peak (15 to 30 minutes after intramuscular injection) or constant (with the intravenous drip method) blood serum levels of penicillin expressed in units per ml may also be measured and checked against tables giving the expected level for the dose employed Peak levels should range from 2 to 25 units per ml with doses of 60 000 to 500 000 units intramuscularly constant levels between 1 and 10 units per ml with daily doses of 500 000 to 4 million units

A practical method of arriving at the right dosage that has given good results for many years is to start with 100 000 units four hourly and to double the dose every second day until the fever abates the dose to which the patient responds is thus known and is promptly doubled for maintenance purposes and continued for six weeks This method has the advantage of testing the sensitivity of the organism to penicillin *in vivo* and ensuring an adequate therapeutic maintenance dose The theoretical objection that it might breed penicillin resistant organisms has not been substantiated in practice

To avoid the discomfort of frequent needling there is an increasing tendency to give massive doses of penicillin (0 25 to 0 5 mega unit) three or four times daily As these massive doses have a penetrating power denied to more modest quantities there is something to be said for this method but they should not be given too infrequently

Another way of avoiding such frequent injections is to use one of the longer acting penicillins such as procaine penicillin As an aqueous suspension this may be injected intramuscularly in doses of 600 000 units twice daily It should never be u ed at the start however and is only advised later in cases that have responded quickly and dramatically to the minimum daily dose of sodium penicillin G

Finally the blood level of penicillin may be increased up to fourfold by the oral administration of certain substances such as benzoic acid (Bronfenbrenner and Favour 1945) sodium benzoate or caronamide (4 carboxy phenylmethane sulphonanilide) which interfere with penicillin excretion by the renal tubules The dose of each of these substances is 2-3 G four

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Heart failure should be treated in the customary fashion but the prognosis is grave in these cases

Diffuse glomerulo nephritis may be mistaken for a relapse of bacterial endocarditis If the renal function is impaired the blood level of penicillin may rise considerably and thus aid the primary treatment unfortunately, however the nephritis usually proves fatal According to Spain and King (1952) diffuse glomerular nephritis rarely occurs if treatment is started within the first two months of the illness

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hourly (Boger *et al*, 1948) Caronamide may be combined with sodium benzoate with some advantage and is a valuable adjunct to treatment in highly resistant cases Probenecid (Benemid) now seems to be replacing caronamide the dose is 0 5 G six hourly

*Treatment of relapses or resistant cases* If the previous course of treatment was inadequate in dosage or duration the standard course of 2 mega units daily for six weeks should be instituted but if a relapse follows adequate treatment every effort should be made to culture the organism and to determine its sensitivity to penicillin If its resistance is not greater than eight times the standard the dose of penicillin should be doubled and treatment should be continued for six weeks If the coefficient of resistance is greater than 8 the dose of penicillin should be increased proportionately If the organism is highly resistant or if it has not been isolated and the infection remains uncontrolled streptomycin may be tried The dose is 1 G twice daily for two weeks followed by 1 G daily for four more weeks Caronamide does not influence the blood level of streptomycin, for the latter is excreted by the glomeruli

Combined penicillin and streptomycin treatment is advised for enterococcal infections (Hunter 1947 Geraci and Martin 1954) The dose of penicillin in these cases should be at least 10 million units daily (Hunter 1953)

Innumerable reports of resistant cases of bacterial endocarditis caused by a wide variety of organisms have appeared in the literature in recent years and the majority have responded in the end to one or other of the newer antibiotics when given in sufficient doses To review all these reports would be profitless The resistant case is a bacteriological problem The organism should be identified and its sensitivity to all available antibiotics tested in the laboratory treatment may then be instituted on a proper foundation

*Toxic reactions of penicillin* Apart from local pain from subcutaneous or superficial intramuscular injections and phlebothrombosis from intravenous injections the only toxic manifestations which can be attributed to penicillin are fever and urticaria Fever was common when crude penicillin was used but is rarely seen nowadays Urticaria develops in about 5 per cent of cases and may be extreme soft tissue œdema and hydrarthrosis are occasionally associated This allergic reaction is alleviated by adrenaline and by the antihistamine group of drugs Penicillin may be continued in mild cases but may have to be stopped if the reaction is severe or the dose may have to be reduced

The chief toxic effect of streptomycin is on the vestibular nerve loss of the sense of balance may be permanent if heavy doses are continued after giddiness has developed A conservative dose of 1 G daily however may be continued in the presence of minor vestibular symptoms if the latter are controlled by means of antihistamine drugs

*Other considerations* An infected ductus should be controlled by penicillin then ligated as soon as the patient is fit enough

CHAPTER XIII

# PERICARDITIS

THE features of pericarditis depend upon its etiology the presence or absence of effusion the nature and hydrostatic pressure of such effusion and the development or otherwise of constriction in chronic or adhesive cases

## ETIOLOGY

Pericarditis may be benign rheumatic tuberculous pyogenic allergic traumatic uræmic or secondary to myocardial infarction malignant growths may invade the pericardium hæmopericardium may result from rupture of a syphilitic or dissecting aneurysm from perforation of a myocardial infarct or ventricular aneurysm or from stab or gun shot wounds of the heart hydropericardium may complicate congestive heart failure or myxœdema sometimes the etiology is obscure All these types have their own special characteristics which will be described subsequently but they have also certain features in common

### *DRY (FIBRINOUS) PERICARDITIS*

All varieties of pericardial inflammation may present in this form The diagnosis rests on three cardinal signs pain pericardial friction and a specific electrocardiographic pattern Disturbances of temperature pulse rate sedimentation rate etc of course may occur but are of little help in diagnosis

*Pain* Capps (1932) found that the pericardium was insensitive to stimuli calculated to produce pain except in that part of it roughly its lower third which is supplied by the phrenic nerve It follows that pericarditis should be painless unless the pain has phrenic distribution or unless it is pleural in type from secondary involvement of that structure In fact this is only partly true in many cases there is no pain in some pain is referred to the neck or shoulder tip in others it is precordial and pleural in type catching the breath on inspiration or on coughing but not infrequently the pain has none of these characteristics being præcordial constant sharp in quality and uninfluenced by respiration pericardial pain of this type may be aggravated by rotating the trunk or by swallowing (McGuire Kotte and Helm 1954)

*Pericardial friction* Friction sounds may be heard anywhere over the heart according to the site and nature of the pathological process but are most common at the left sternal border in the fourth intercostal space over the area of maximum cardiac dullness where the pericardium lies in contact with the chest wall They are superficial rough or smooth loud or

soft their timing is peculiar being out of step with the heart sounds Sometimes they are confused with the to and fro murmur of aortic valve disease or with artificial stethoscopic sounds sometimes they escape detection Pleuro pericardial friction can usually be distinguished by its relationship to respiration

*Electrocardiographic changes* A diagnostic electrocardiographic $T_2$ pattern first described by Porte and Pardee (1929) may be found in the majority of cases of genuine pericarditis whatever the etiology and whether

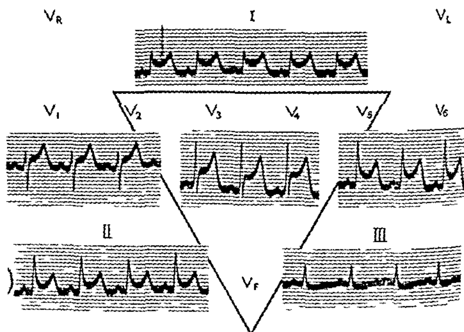



Fig 13 01—Electrocardiogram showing the early phase of the pericardial $T_2$ pattern This graph is atypical in that the R T segment is not elevated in lead 3

or not there is effusion (Wood 1937) It develops in two stages early and late the changes usually appearing in all leads and therefore especially in lead 2 In the early phase (fig 13 01) the RS-T segment is elevated but retains its natural concavity Within a few days it regains the iso potential level or becomes depressed and the T wave becomes flattened diphasic, or inverted (fig 13 02) QRS remaining unchanged throughout or losing voltage When the inflammation subsides the graph returns to normal except when a tuberculous pericarditis merges into the chronic constrictive form, when flat or inverted T waves and low voltage QRS complexes become permanent The T pattern may only be appreciated in serial electrocardiograms, because changes may be confined to leads 1 and 2 in one record, and to leads 2 and 3 in another Similar appearances are seen in all chest leads and may be found when limb leads are normal (fig 13 03)

I

$V_1$ $V_2$ $V_3$ $V_4$ $V_5$ $V_6$

II $V_F$ III

21ST JUNE 46

I

$V_1$ $V_2$ $V_3$ $V_4$ $V_5$ $V_6$

II $V_F$ III

4TH JULY 46

Fig 13 02—Electrocardiogram showing the later phase of the pericardial $T_2$ pattern case of pyogenic pericarditis secondary to bronchopneumonia

Both early and late stages appear to be due to alterations in the biophysical properties of the sub epicardial myocardium, whether or not there are recognisable structural changes (Kisch *et al* 1940) The early pattern of generalised pericarditis may be distinguished from that of myocardial infarction by the absence of a conspicuous Q wave by the preservation of the upward concavity of the RS T segment and by the occurrence of maximum RS T deviation in lead 2 (cf $T_1$ and $T_3$ types in myocardial infarction) When pericarditis is localised however changes may be maximum in leads 1 or 3 (Burchell Barnes and Mann 1939) The later stage

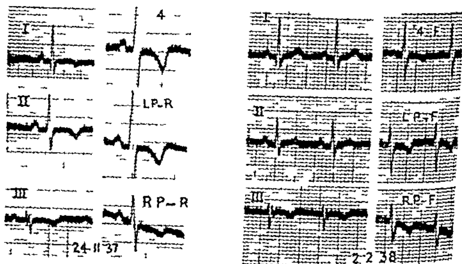



Fig 13 03—Electrocardiogram showing late changes due to pericarditis in the second record (2nd February 1938) they are limited to the chest leads

may be confused with isolated myocarditis myxœdema carbon monoxide poisoning severe anæmia and most of the cardiopathies described in the previous chapter On the other hand the characteristic initial phase, the changing picture in serial graphs and the clinical features of the case usually make the diagnosis easy

## PERICARDIAL EFFUSION

Fluid in the pericardial sac may be a simple transudate (hydropericardium) a straw coloured sterile exudate a purulent exudate or blood (hæmopericardium) It may disturb the patient in one or more of four ways (1) stretching of the pericardium may induce præcordial discomfort (2) large effusions exerting pressure on surrounding structures especially on the bronchi and lungs may produce reflex cough and dyspnœa (3) if the fluid is purulent there may be constitutional effects similar to empyema, (4) as the pressure rises in the pericardial sac cardiac filling is hampered the pressure rises in both venous systems the ventricular stroke output diminishes and the blood pressure tends to fall The raised venous

pressure is partly beneficial for it aids cardiac filling the diminished stroke volume is countered by tachycardia reflex vasoconstriction serves to maintain the blood pressure (Stewart Crane and Deitrich 1938) When these compensatory adjustments fail to meet the circulatory demands the situation becomes critical (cardiac tamponade) There is reason to believe that cardiac tamponade seriously interferes with the coronary blood flow not only because the cardiac output is reduced and the blood pressure low but because the pressure gradient between the aorta and coronary circulation is significantly reduced The myocardium appears to suffer accordingly and true heart failure may result This may explain those cases that fail to recover after decompression and suggests that tamponade should be regarded as a medical emergency

*Clinically* the *pulse* may be normal small or paradoxical according to the intra pericardial pressure During inspiration descent of the diaphragm stretches the already tense parietal pericardium and increases the pressure within it cardiac filling is then impaired and the stroke output and pulse pressure fall As in constrictive pericarditis it is easier for the heart to increase its output by means of tachycardia than by raising the venous filling pressure

The venous pressure varies directly with the intrapericardial pressure and may rise appreciably during inspiration (Kussmaul s sign) The jugular pulse usually shows a rapid v descent and conspicuous y trough as in Pick s disease

Effusions in excess of 250 ml may be detected by *percussion* Dullness may be elicited in the second left space when the patient lies flat to the left of the apex beat when the latter can be located in the xiphisternal angle and to the right of the sternum in the 4th and 5th intercostal spaces (Rotch s sign 1878)

*Auscultation* reveals pericardial friction in the majority of instances even with gross effusions The first heart sound is soft because late diastolic ventricular filling is virtually at a standstill and the atrio ventricular valves are therefore more or less closed before the ventricles contract the second sound is soft because the blood pressure is low The fluid layer between the heart and chest wall may also damp the sounds but this is less certain Theoretically an accentuated third heart sound might be expected in view of the rapid ventricular filling in early diastole but it is rarely heard

Dullness to percussion and bronchial breathing at the left base usually attributed to collapse of the lung (Ewart 1896) are more likely to be due to associated pleural effusion at least in rheumatic cases (Thomas Besterman and Hollman 1953)

*Fluoroscopy* reveals a large relatively still cardiac silhouette with the natural contours of individual chambers obliterated (fig 13 04) It is doubted whether any of the special radiological points that have been said to favour effusion are really tenable e g short vascular pedicle divergent vascular shadows at the base change of shape with alteration of posture

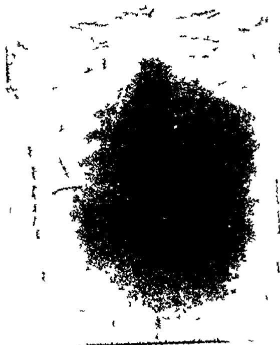


Fig 13 04—Skiagram of a case of pericardial effusion



(a) Before treatment



(b) Two weeks later

Fig 13 05—Gross pericardial effusion

acute right cardio phrenic angle and convex posterior inferior cardio phrenic angle in the first oblique position (Besterman and Thomas 1953) Rapid changes in the size of the cardiac shadow are more reliable (fig 13 05) but even these may be seen in cases of acute dilatation of the heart with rapid recovery Since more accurate methods of diagnosis have been adopted there have been many surprises the more common error has been to mistake pericardial effusion for cardiac enlargement but the reverse has also been true

There are three good ways of determining the presence and degree of pericardial effusion—*cardiac catheterisation* angiocardiography and paracentesis If a cardiac catheter is looped in the right atrium its tip may be



Fig 13 06—Catheter looped in the right atrium proving the absence of pericardial effusion

rotated laterally and guided up and down the lateral wall of the right atrium When there is no effusion the tip of the catheter is then separated from the transfucent lungs only by the thin wall of the right atrium (fig 13 06) When there is pericardial effusion however the tip of the catheter is separated from the lungs by an opaque band of fluid (Wood 1950 1951) If 10 to 20 ml of diaginol are injected rapidly through the catheter when its tip is directed upwards against the lateral wall of the right atrium and a film is exposed towards the end of the injection, the degree of effusion can be estimated accurately (fig 13 07) Routine *angiocardiography* (Williams and Steinberg 1949) reveals the degree of pericardial effusion with greater precision (fig 13 08) but may be undesirable when the alternative diagnosis is severe heart failure *Paracentesis* may prove the presence of effusion but only indicates its degree if all the fluid is removed or if sufficient air is introduced The safest of these three methods is

atrial catheterisation This does not, of course, distinguish pericardial effusion from gross dilatation of the left atrium

The *differential diagnosis* of pericardial effusion includes any general cardiac enlargement of uncertain nature heart failure from rheumatic carditis or any of the more obscure cardiopathies described in Chapter XI and certain congenital anomalies such as Ebstein s disease Under the clinical circumstances the best indication of pericardial effusion is a friction rub and the best evidence of cardiac dilatation is loud diastolic gallop rhythm A paradoxical pulse certainly favours effusion but too much reliance should not be placed on Kussmaul s sign the presence or absence of a palpable cardiac impulse the intensity of the heart sounds or inverted T waves in the electrocardiogram for all these may occur in either condition



Fig 13 07—Pericardial effusion seen beyond the right atrial border which is delineated by the tip of a looped catheter through which a jet of diodone has been injected

In addition to the three semi radiological methods of diagnosis described above certain physiological tests may prove useful although they have not been tested sufficiently yet These include Valsalva s manœuvre and the effect of alterations of posture on the cardiac output and therefore on the blood pressure pulse rate forearm blood flow and digital pulse In pericardial effusion the physiological response to the Valsalva manœuvre should be normal i e the period of strain should be followed by a rise of blood pressure and slowing of the pulse whereas in heart failure these changes do not occur Tilting the patient foot down lowers the venous pressure in pericardial effusion this should lower the cardiac output and so diminish the blood pressure and pulse pressure increase the heart rate reduce the forearm blood flow and diminish



Fig 13 08—Angiocardiogram demonstrating pericardial effusion

the digital pulse in heart failure, lowering the venous pressure increases the cardiac output and therefore has the opposite effect on the phenomena mentioned The essential principle underlying all physiological tests for pericardial effusion is that the heart behaves normally (Isaacs Berglund and Sarnoff 1954) whereas cardiopathies with considerable cardiac dilatation are overloaded

Cardiac catheterisation in both pericardial effusion and most of the obscure cardiopathies reveals that pulmonary venous and left atrial pressures are raised to just about the same level as the right atrial pressure in Ebstein s disease of course this is not so

*Treatment* The object of treatment is to prevent death from cardiac tamponade and is achieved by avoiding therapeutic agents that may lower the venous pressure such as *mersalyl a low sodium diet and venesection* and by decompression if necessary In practice it is rarely necessary to tap a pericardial effusion for critical tamponade is rare in medical cases The combination of a small pulse venous pressure over 10 cm of water at 90 degrees and systolic blood pressure below 90 mm Hg provides the necessary indication Paracentesis may be carried out to the left of the apex beat, or at any point where there is reason to believe there is plenty of fluid If the needle touches the heart forcible pulsation can be felt and it should be withdrawn a little or inserted elsewhere with due care the risk of causing hæmopericardium from puncturing a coronary vessel is small Fluid may also be removed if purulent or if untoward symptoms are caused by pressure on surrounding structures Traumatic hæmopericardium which is responsible for many cases of tamponade requires surgical evacuation and repair of the underlying injury

## *CHRONIC CONSTRICTIVE PERICARDITIS*

Although Richard Lower described the paradoxical pulse and calcified pericardium as early as 1669 he was not in a position to grasp their full significance and it was Chevers who really drew attention to the disease giving an excellent account of it with considerable understanding of the circulatory dynamics involved in 1842 The term Pick s disease is unfortunate for Pick (1896) merely emphasised the accompanying pseudo cirrhosis of the liver and because priority undoubtedly goes to Chevers The issue is best avoided by adhering to the descriptive title—chronic constrictive pericarditis

*Morbid anatomy* The condition may be regarded as a complication of the healing process following tuberculous and perhaps certain other forms of pericarditis the fibrous tissue laid down so extensively in the active phase contracting on maturation and limiting diastolic expansion of the heart Calcium is often deposited in large quantities and the whole heart may become encased in stone

*Etiology* Tuberculosis accounts for at least three quarters of the cases and may still be active when constriction first develops The

bacteria appear to be responsible for a few and the cause is uncertain or unknown in the remainder None are rheumatic (White 1935) Some regard tuberculosis as the sole cause of chronic constrictive pericarditis (Andrews Pickering and Holmes Sellars 1948)

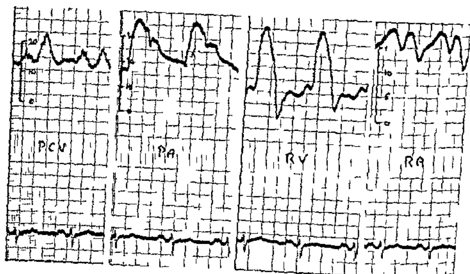



Fig 13 09—Intracardiac pressure pulses from a case of Pick's disease

*Hæmodynamics*

The essential physiological fault in Pick's disease is inadequate cardiac filling. It is uncertain to what extent ventricular contraction is also hampered but that it is so in some measure can scarcely be doubted The rigid limit imposed on diastolic filling is more or less the same for both ventricles so that the rise of pressure in the two venous systems is always similar (if not identical) This was true in all of eight consecutive cases that we have investigated and in a series of six cases reported by Dexter's group (Sawyer *et al*, 1952) The elevated atrial and venous pressures usually measure between 10 and 20 mm Hg above the sternal angle (fig 13 09) As a rule the dominant wave is the y descent and trough (fig 13 10) This represents the sudden fall in venous pressure that follows the opening of the tricuspid valve when blood pours into the momentarily relaxed right ventricle Owing to the unyielding pericardium the right ventricle is filled to its maximum

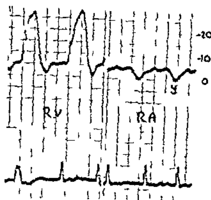



Fig 13 10—Typical right atrial and right ventricular pressure pulses in a case of Pick's disease showing conspicuous y troughs

capacity very quickly and both right ventricular and right atrial diastolic pressures therefore rise again smartly The right ventricular pressure pulse is characterised by a conspicuous dip in early diastole which is the counterpart of the y trough in the venous pulse The same phenomenon may be recorded in left atrial and left ventricular pressure pulses (fig 13 11) Typical tracings have been published and discussed by Bloomfield *et al* (1946) Eliasch Lagerlof and Werko (1950) Hansen *et al* (1951) and McKusick (1952)

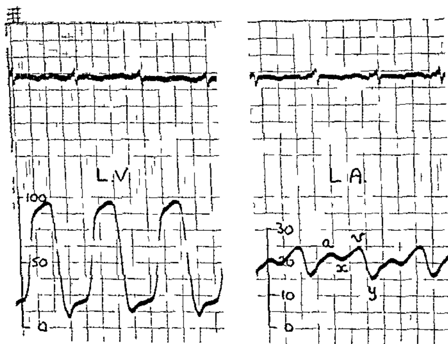



Fig 13 11—Left atrial and left ventricular pressure pulses from a case of Pick's disease

Since the stroke output is strictly limited and more or less fixed alterations of cardiac output per minute depend chiefly on changes in heart rate (Stewart and Heuer 1939) Raising or lowering the venous pressure makes relatively little difference Since maximum filling is accomplished very quickly doubling the heart rate may almost double the minute output

The Valsalva manœuvre may give rise either to a normal or to a square wave response (fig 13 12) and may therefore fail to distinguish constrictive pericarditis from heart failure It is presumed that an intrathoracic pressure of 40 mm Hg may fail to compress the calcified box that encloses the heart The assumption that cases giving a square wave response are really in a state of myocardial failure is unwarranted on the other ha

is not denied that true heart failure may occur, and can sometimes be demonstrated post operatively

Other physiological phenomena such as Kussmaul's sign and pulsus paradoxus are discussed with the physical signs

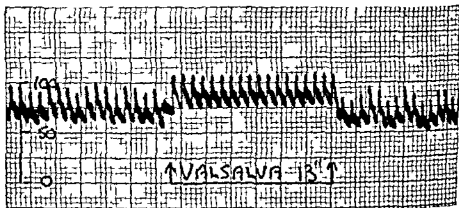



Fig 13 12—Valsalva manœuvre in a case of Pick s disease showing a square wave response in the arterial pressure pulse

*Clinical features*

The patient may be of either sex and almost any age but is usually an adult between 20 and 50 A previous history of tuberculous pericarditis or peritonitis is unusual

The onset of symptoms is insidious and signs may be well developed when the patient complains of little beyond fatigue slight breathlessness on effort fullness of the abdomen and perhaps a tendency to œdema Obvious ascites and dropsy are late symptoms although they may be the first that make the patient seek medical advice Cases with active tuberculous pericarditis of course are in a different category

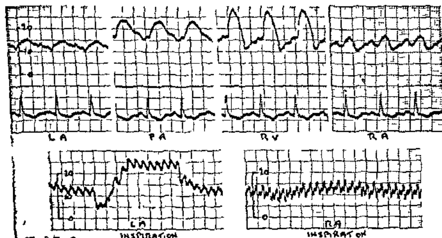
On examination the pulse is rather small and sometimes paradoxical almost disappearing with inspiration This is due to interference with cardiac filling when the pericardial tension is increased by descent of the diaphragm although it is the forward counterpart of Kussmaul s sign (*vide infra*) it is far less common The blood pressure is usually low The venous pressure is high and may rise appreciably during inspiration (Kussmaul 1873) A similar inspiratory rise of left atrial and pulmonary venous pressures may be recorded with the wedged catheter technique (fig 13 13) The chief wave in the venous pulse (fig 13 10) is usually the *y* trough (Friedreich s sign 1864) but in relatively mild cases with normal rhythm the *x* descent may be equally conspicuous Atrial fibrillation occurs in about one third of all cases its frequency is directly proportional to the age of the patient as in mitral stenosis and thyrotoxicosis

On palpation the heart is usually quiet, the left ventricular impulse

being barely perceptible and there being no lift over the right ventricle There may be an appreciable diastolic shock as if the heart filling rapidly under the influence of a high venous pressure suddenly met the unyielding resistance of a rigid pericardium which from a state of relaxation was thrown abruptly into tension on auscultation this is represented by an



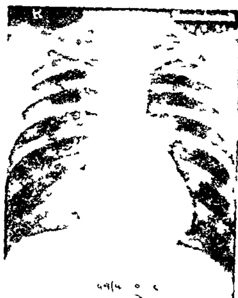

(a) Normal response the pressure falling during inspiration and rising during expiration




(b) Paradoxical response in a case of Pick's disease an even greater rise of pressure is seen in the left atrial pressure tracing

FIG 13 13—Effect of respiration on the left and right atrial pressure

accentuated and early third heart sound (Evans and Jackson 1952) Friction is absent Splitting of the second heart sound may fail to widen on inspiration for increasing the filling pressure of the right ventricle may not augment the stroke volume as previously explained In a minority of cases however not excluding those with the heaviest calcification not only does inspiration delay pulmonary valve closure as in normal individuals but



(a) Anterior view



(b) Calcification seen in second oblique view

Fig 13 14—Skiagrams of a case of constrictive pericarditis

Fig 13 15—Electrocardiogram in a case of chronic constrictive pericarditis

may also increase the intensity of the first heart sound In such cases the Valsalva manœuvre may be expected to give a normal response

Considerable enlargement of the liver ascites and œdema complete the clinical picture

*Fluoroscopy* reveals little cardiac pulsation, the heart shadow is normal in size in 45 per cent slightly enlarged in 17 per cent moderately enlarged in 32 per cent and greatly so in 6 per cent and has an ill defined outline (Paul Castleman and White 1948) Enlargement when present is due to the thickness of the pericardium which may measure as much as 26 mm (Freedman 1939) The shape of the heart shadow is also altered being triangular in half the cases with straight left and right borders and a small or absent aortic knuckle Calcification occurs in about half the cases and is best seen in the left anterior oblique position (fig 13 14)

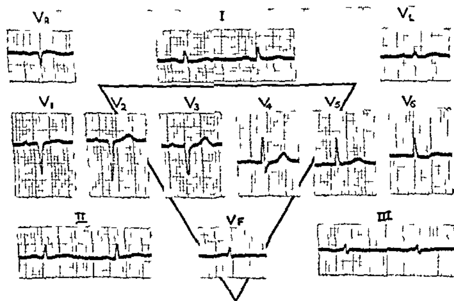



Fig 13 15—Almost normal electrocardiogram from a woman of 67 with Pick disease (proved at operation)

*The electrocardiogram* usually shows low voltage QRS complexes with flattening or inversion of T in most leads representing the late stage of the pericardial $T_2$ pattern which in these cases is permanent (fig 13 15) A conspicuous or bifid P wave is not uncommon Occasionally the electrocardiogram is almost normal (fig 13 16)

*Differential diagnosis* It is insufficiently appreciated that the only pathognomonic sign of chronic constrictive pericarditis is a calcified pericardium and even this can occur without constriction Kussmaul's sign Friedreich's sign a loud and early third heart sound, and the characteristic electrocardiographic pattern can all occur in cases of isolated myocard

or other cardiopathy of clinically obscure origin A paradoxical pulse and the lack of much cardiac enlargement are highly suggestive of Pick's disease under the clinical circumstances but are not pathognomonic and are not necessarily present Poor ventricular pulsation on fluoroscopy is characteristic of most low output states

Because of these difficulties special efforts have been made to find some reliable physiological test that would distinguish Pick's disease without calcification from cardiopathies of clinically obscure nature but on the whole these efforts have failed and many fruitless thoracotomies have been undertaken in consequence This comment applies to intracardiac pressure pulses measurement of the cardiac output in relation to changes of posture and heart rate and the Valsalva manœuvre Unfortunately chronic constrictive pericarditis not infrequently behaves like heart failure and the tests themselves may give indeterminate results

*Treatment* Treatment consists of cardiac decompression achieved by surgical removal of the constricting tissue (Churchill 1929 1936) It has been assumed that the left side of the heart should be freed first to avoid the theoretical risk of acute pulmonary œdema but evidence is accumulating which suggests that constricting forces tend to be distributed equally over both ventricles and that division of constricting bands in any situation may result in generalised diminution of pericardial tension Removal of calcium may be difficult and time consuming but is amply rewarded The chief dangers during the operation are hæmorrhage and cardiac arrest or ventricular fibrillation The post operative course has been smoother since the advent of antibiotics for pulmonary and pleural sepsis can now be avoided or treated effectively The frequency of positive cultures obtained from pericardial tissue removed at operation has proved that activity is no direct bar to surgical treatment but has encouraged the concomitant use of streptomycin Even in subacute cases of tuberculous pericarditis of only six to twelve months duration, pericardiectomy should not be withheld on the grounds of florid activity if mechanical interference with forward flow is endangering life (Andrews Pickering and Sellors 1948)

The results of surgical treatment were good in 62 per cent of 415 cases reviewed by Chambliss *et al* (1951) and may be expected to be so in about three quarters of clinically inactive cases The surgical mortality over the last ten years has fallen from 33 per cent (Sellors 1946) to about 15 per cent (Chambliss *et al* 1951 Evans and Jackson 1952) The oldest patient operated on (successfully) in my own series was 67 years of age

Follow up studies in successfully treated cases reveal improved cardiac filling and forward flow reduction of left and right atrial pressures and disappearance of fatigue dyspnœa ascites and œdema but the physiology of the circulation is still abnormal venous pressures are higher than they should be, Kussmaul's sign may remain the third heart sound may still be heard although it may be softer and appreciably later (Mounsey 1955) normal rhythm is rarely restored the electrocardiogram is usually un

changed and the X ray appearances are much the same although the amplitude of cardiac pulsation may be greater Re constriction presumably as a result of low grade activity has necessitated a second operation in roughly 5 to 10 per cent of surviving cases over a period of 10 to 15 years precise figures on this point are not yet available

## ADHERENT PERICARDIUM

During the first quarter of this century adherent pericardium was still considered an important complication of pericarditis Extensive adhesions anchoring the heart to adjacent resistant structures were believed to add a heavy burden to ventricular systole The theory was coloured by the pathological observations of Cabot (1926) who recorded gross cardiac enlargement associated with rheumatic adherent pericarditis The clinical picture included Broadbent s sign (indrawing of the postero lateral aspect of the ribs during ventricular systole resulting from fixation of the visceral pericardium to the diaphragm) paradoxical pulse diastolic shock or rebound of the ribs fixation of the apex beat so that it failed to shift with change of posture similar fixation of the electrical axis of the heart and unexplained cardiac enlargement To cure this unhappy condition the operation of cardiolysis (Brauer 1903) was devised to free the heart of its encumbrances by dividing adhesions between it and the surrounding tissues and especially by extensive rib resection so that the heart could pull against less resistant structures In more recent years, however, the serious consequences of adherent pericardium have been denied, and its surgical treatment is no longer favoured

Hosler and Williams (1936) failed to produce any cardiac enlargement or alteration of cardiac function by suturing the heart and pericardium to the diaphragm in 13 dogs nor could they find a single instance of cardiac enlargement in 76 cases of adherent pericarditis in which there was not an adequate organic intracardiac cause chiefly valvular disease Similar clinical and autopsy evidence was obtained by Armstrong (1940) in 72 cases and by Evans (Parkinson 1936) in 49 cases

All Cabot s cases of gross cardiac enlargement with adherent pericardium were complicated by serious valve disease Although Broadbent s sign (if not confused with indrawing of the left antero lateral aspect of the thorax which may occur whenever the heart is grossly enlarged) and diastolic rebound of the ribs are reliable signs of extrapericardial adhesions paradoxical pulse favours constriction and fixation of the apex beat or of the electrical axis is too variable to be of diagnostic value (France 1938)

## TYPES OF PERICARDITIS BASED ON ETIOLOGY

*Rheumatic pericarditis* The dry form may give rise to nothing more serious than transient pericardial friction but it has an important bearing on diagnosis its advent during the course of rheumatic fever proving

beyond question the presence of active carditis More extensive pericarditis is usually associated with gross rheumatic infection so that serious carditis may be assumed These patients are often very ill, with high fever considerable dyspnœa or hyperpnœa, and much pain The development of cardiac dilatation and failure under similar circumstances is apt to be mistaken for pericardial effusion with cardiac compression and indeed the differential diagnosis may not be easy The position of the apex beat the ease with which it can be felt and the presence or absence of dullness in the second left intercostal space are good guides but the electrocardiogram may be indeterminate and the interpretation of skiagrams difficult (see page 488) Occasionally special diagnostic techniques may be necessary The safest of these is right atrial catheterisation (page 663) Angiocardiography is equally conclusive but less safe in these very sick children The results of paracentesis should be interpreted with more caution fluid may be obtained when there is a trivial amount present and failure to obtain fluid may be due to technical fault

Rheumatic pericardial effusion is a clear straw coloured sterile exudate it rarely compresses the heart tends to be resorbed spontaneously without undue delay appears to respond to salicylates and is usually best left alone

Fortunately there are no significant after effects for chronic constrictive pericarditis is never rheumatic and adherent pericardium though not uncommon is of little importance Pericardial calcification is seen occasionally but is scanty and harmless

Treatment is limited to relief of pain when present and to cardiac decompression in rare cases of high pressure effusion For the former antiphlogistine is comforting but when the pain is severe morphine should be given For the latter paracentesis is required and should be repeated when necessary Salicylates may also help Otherwise treatment should be directed towards the rheumatic illness as a whole

*Tuberculous pericarditis* Tuberculous pericarditis is uncommon in Great Britain it affects all age groups but favours coloured races and the male sex The infection usually spreads from mediastinal lymph gland or pleura (Peel 1948) Effusion is the rule and if the patient survives constriction may follow The onset is insidious and in cases with effusion a large quantity of fluid may collect before symptoms are noticed Dyspnœa and an irritable dry cough due to pressure on the lungs and bronchi are the usual complaints The absence of constitutional disturbances is often remarkable but continued fever anorexia loss of weight night sweats and secondary anæmia may occur in the more active cases Diagnosis depends upon the absence of rheumatic manifestations the subacute or chronic course of the malady the discovery of tuberculosis elsewhere and the results of culture and guinea pig inoculation of specimens of fluid obtained by paracentesis The effusion is usually a clear straw coloured exudate containing lymphocytes but is sometimes blood stained Occasionally the effusion is encapsulated and resembles a pericardial cyst radio-

logically (Freedman 1937) a tuberculous pericardial abscess presents a similar appearance The course is prolonged usually ranging between three and eighteen months and is often downhill with progressive emaciation toxæmia and anæmia cardiac compression may become dangerous, when frequent tapping adds to the patient s misery

It is doubtful if more than 20 per cent of untreated cases with positive cultures survive and of these the majority develop chronic constrictive pericarditis subsequently not infrequently active and constrictive stages are telescoped The prognosis is very different when tubercle bacilli cannot be recovered from the pericardial fluid the mortality rate being then less than 10 per cent (Harvey and Whitehill 1937) but of course the etiological diagnosis in many of these cases is open to question and very few constrict later Out of 71 untreated cases of tuberculous pericarditis reported by Carroll (1951) 53 5 per cent died within two years

Treatment with streptomycin 1 G intramuscularly daily or 2 G every third day in conjunction with para aminosalicylic acid (PAS) or its sodium alt 5–10 G twice daily by mouth or with isoniazid 100 mg twice daily by mouth for four to six months has reduced the mortality from at least 50 per cent to 15 per cent in proved cases (Goyette Overholt and Rapaport 1954) The immediate results of such treatment are good in 70 per cent of cases but it is too soon to assess the frequency of subsequent constriction It is already evident however that constriction is the rule if treatment is delayed more than four months from the recognised onset of the disease

*Polyserositis* Whilst tuberculosis may affect the pleura and peritoneum as well as the pericardium the term polyserositis (Concato s disea e) is usually reserved for a somewhat similar inflammatory process of unknown origin Large effusions collect in the serous sacs the fluid being a clear or opalescent straw coloured sterile exudate The process is obliterative and in the pleural cavity paracentesis must be performed ever higher as the two layers of pleura become fused together in a thick dense white matting Over the liver and spleen the greatly thickened peritoneum resembles a stout coating of sugar ice. When the pericardium is involved resorption of fluid is followed by total obliteration of the pericardial cavity and con striction may ensue The course and prognosis are similar to those of tuberculous pericardial effusion

*Benign (idiopathic) pericarditis* Idiopathic pericarditis has been recog nised for at least a century (Christian 1951) The newer title *benign pericarditis* (Logan and Wendkos 1948) has the advantage of emphasising its most important feature

The M/F sex ratio is 3 1 The patient may be young middle aged or elderly with almost equal frequency the average age is 35 years About two thirds of reported cases have developed after an average latent period of twelve days following an upper respiratory tract infection (McGuire *et al* 1954) The onset is usually acute with fever malaise pericardial pain friction leucocytosis and raised sedimentation rate Effusion

develops in about two thirds of all cases but is rarely extensive The fluid is usually a straw coloured sterile exudate containing 3 to 4 G of protein per cent and a variable number of lymphocytes The electrocardiogram nearly always shows the typical changes of pericarditis

The course averages about six weeks with a range of two weeks to three months but nearly 20 per cent relapse occasionally several times the intervals between attacks varying between two and eight weeks This relapsing tendency is similar to that seen in traumatic and post operative pericarditis

Recovery is finally complete without calcification or constriction (Carmichael *et al* 1951) subsequent Pick s disease suggests that the initial diagnosis was wrong

In differential diagnosis benign pericarditis can usually be distinguished from cardiac infarction by the antecedent history of upper respiratory tract infection malaise and fever preceding pain the special characteristics of pericardial pain an early extensive and persistent friction rub, the development of pericardial effusion and the absence of abnormal Q waves in the electrocardiogram

No treatment has so far proved effective, although most of the newer antibiotics have been tried

*Malignant infiltration of the pericardium* When a male over 40 years of age complains of recent cough and breathlessness of insidious onset and is found to have a large pericardial effusion a malignant or tuberculous etiology is probable If there is no fever and the fluid is blood stained the diagnostic scales tip sharply in favour of malignancy When the pericardium is extensively invaded hæmorrhagic effusion and cardiac tamponade are the rule but when it is infiltrated by a single small nodule the fluid is usually clear and straw coloured and the sac being more distensible tamponade is less frequent The condition is invariably fatal and death never long delayed Autopsy usually reveals a primary bronchial carcinoma

*Pyogenic pericarditis* Streptococcal pneumococcal and staphylococcal infection may each give rise to pericarditis Fever leucocytosis and toxæmia are more conspicuous than in other forms Effusion is common and usually purulent It is generally believed that recovery may be followed by constriction, but this is certainly unusual if it occurs at all Streptococcal pericarditis may complicate tonsillitis erysipelas broncho pneumonia or any other streptococcal infection It usually occurs during the acute stage of the illness and is then readily distinguished from rheumatic pericarditis but when there is an appreciable latent interval this distinction is not so easy Pneumococcal pericarditis is usually a complication of left basal pneumonia organisms gaining access to the pericardium by direct spread from the pleura Staphylococcal pericarditis may complicate myocardial abscess from staphylococcal septicæmia

The course and prognosis of pyogenic pericarditis have been radically altered by chemotherapy Penicillin is more effective than the sulphona

mides and should be given in divided doses of 1 mega unit daily for seven to ten days Surgical drainage is only necessary when there is frank suppuration With such treatment initial recovery is the rule but the ultimate outcome is uncertain The lower mortality rate may result in an increased incidence of chronic constrictive pericarditis on the other hand the prevention of frank suppuration may have the opposite effect The few cases so far followed up by the author have not constricted

*Hæmopericardium and traumatic pericarditis* Hæmorrhage into the pericardial sac may be caused by stab or gun shot wound by rupture of a syphilitic or dissecting aneurysm of the aorta or by perforation of a myocardial infarct or ventricular aneurysm Wounds of the heart are not necessarily fatal and if the patient survives the initial insult relief of cardiac tamponade and surgical repair may be life saving Rupture of the heart or aorta into the pericardium is always fatal but not necessarily immediately A patient with a perforated infarct, for example may live as long as ten days

Severe blows crush injuries or blast may cause myocardial bruising and pericardial ecchymoses Transient pericardial friction and characteristic electrocardiographic changes usually provide evidence of the lesion If there is no damage to the superficial coronary arteries complete recovery is the rule

An interesting form of traumatic pericarditis may be due to pericardial foreign body (usually a metallic fragment) or to a foreign body lying close to the pericardium In these cases recurrent attacks of pericarditis with clear sterile effusion may occur at any time up to four months after the original injury The interval between attacks is usually two to six weeks during which the patient seems perfectly well The attacks themselves which last about a week tend to be severe with fever rapid effusion cardiac tamponade and considerable pain and distress Of seven cases that I reported in 1945 however, none died If the foreign body is easily accessible it is best removed in a quiescent period if not it may be safer to leave it *in situ*

*Post operative pericarditis* may follow any direct operation on the heart including mitral valvotomy aortic valvotomy via the left ventricular route pulmonary valvotomy and infundibular resection Its frequency is about 10 per cent Pericardial pain and fever usually lasting about a week are the chief manifestations pericardial friction common enough during the first week or two may reappear and a small effusion may develop The first episode usually occurs during the third or fourth post operative week sometimes just after the patient has been discharged from hospital Attacks are apt to be recurrent with intervals of two to three weeks over a period of two or three months

The syndrome is sharply reminiscent of the recurrent pericarditis associated with pericardial foreign body described above and may well be traumatic in nature (Wood 1954)

*Uræmic pericarditis* Pericardial friction is not uncommonly heard in patients dying with uræmia Symptoms are rare effusion absent, and electrocardiographic changes minimal At autopsy needle like crystals of urea may be found massed in the pericardium



Fig 13 17—Pericardial effusion of three years duration in a case of extreme essential hyper tension

*Pericarditis secondary to myo cardial infarction* Acute myo cardial infarction may give rise to a local (60 per cent) or general (15 per cent) pericardial re action, and perforation may lead to hæmopericardium Local pericarditis is limited to the sur face area of the infarct gives rise to no symptoms and does not interfere with the electrocard iographic pattern of the under lying lesion A fleeting friction rub may be heard if the infarct is anterior

General pericarditis is less common but more important, it may cause additional pain allows anterior friction to be associated with po terior infarction (Stewart and Turner 1938) influences the electrocardiographic pattern and may even give rise to effusion

*Chronic idiopathic pericardial effusion* Large pericardial effusions of unknown cause may remain virtually unchanged for years It seems more than a coincidence that in my own series of six such cases all had hype tension two of them malignant The effusion was usually gross (fig 13 17) and had lasted for at least three or four years in four of them There was no fever pain leucocytosis or raised sedimentation rate indeed, the effusion was virtually silent in all of them and in the two cases of maligna t hypertension seemed to have prevented serious dyspnœa and orthopnœa by limiting the inflow to the right ventricle In the case illustrated for instance the intrapericardial pressure was 9 cm of saline and the venous pressure was raised proportionally the patient was able to lie flat and could even be tilted head downwards without distress after paracentesi orthopnœa and paroxysmal cardiac dyspnœa developed within three or four days and had to be controlled by dehydration until the pericardial effusion reaccumulated

The fluid in these cases has always been clear and acellular but has contained at least 4 G of protein per cent

*In cases with severe hypertension it may be best not to disturb the* physiological situation unless the blood pressure can be well controlled In cases without serious hypertension however partial pericardiectomy should be advised if the effusion is gross and chronic Mr W C Cleland undertook this operation in one of my cases at the Brompton Hospital after

repeated tapping and dehydration had failed to prevent rapid reaccumulation of fluid (fig 13 05) The condition had been present for at least four years and possibly for ten years The pericardium itself looked normal enough and there has been no trouble since

Chronic effusive pericarditis may also occur in children a good example in which the effusion was observed over a period of four years was reported by Contro *et al* (1955) in a child of 7 to 11

*Hydropericardium* Hydropericardium associated with congestive failure is rarely conspicuous and is of little clinical significance Pericardial effusion may also complicate myxœdema when it frequently contains cholesterol (Creech *et al* 1955)

*Pericardial cyst* A rounded opacity deforming the border of the heart shadow may represent a fibroma lipoma hydatid cyst cardiac aneurysm hæmatoma loculated pericardial effusion cold abscess or pericardial diverticulum or cyst

Cardiac tumours usually alter the electrocardiogram and interfere with cardiac function hydatid disease can be recognised by Casoni and complement fixation tests cardiac aneurysm by paradoxical pulsation and characteristic electrocardiogram hæmatoma by the history of stab or gunshot wound and localised tuberculous abscess by subacute pericardial pain and local electrocardiographic changes A pericardial cyst or diverticulum, however is silent does not disturb the electrocardiogram and is discovered only on routine radiography (fig 13 18) It may be safely disregarded

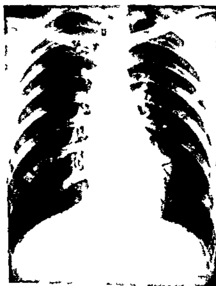


Fig 13 18—Pericardial cyst or diverticulum on the left border of the heart

Mediastinal tumours are more likely to be confused with aortic aneurysm and are therefore considered in the next chapter

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CHAPTER XIV

# SYPHILITIC AORTITIS

SYPHILITIC inflammation of the aorta is clinically unrecognisable unless it results in fusiform dilatation saccular aneurysm aortic incompetence angina pectoris or possibly heart block It is true that many museums contain a specimen of syphilitic myocarditis and even of syphilitic endocarditis but these are oddities The various manifestations of syphilitic aortitis commonly appear from ten to thirty years after primary infection, usually between the ages of 30 and 60 account for about 3 per cent of all cases of organic heart disease in Britain and are approximately five times more common in men than in women Aortic incompetence is about twice as common as aneurysm

There can be little doubt that the disease is becoming less frequent and will become rare This is the result of educating the public in venereology and the improved treatment of early syphilis Thompson Comeau and White (1939) found cardiovascular syphilis had developed clinically in 10 per cent of 241 patients known to have had syphilis fifteen to twenty five years previously all had been inadequately treated by 1939 standards Uncomplicated aortitis rarely recognised except at necropsy is undoubtedly more frequent but its exact clinical incidence is difficult to assess published figures depending on the criteria upon which the diagnosis rests According to Moore only 16 per cent of 105 cases of uncomplicated syphilitic aortitis proved at necropsy were recognised clinically prior to 1932 (Moore *et al* 1932) whereas 68 per cent of 79 proved cases were correctly diagnosed in life between 1932 and 1941 (Mattman and Moore 1943) He ascribed this improved diagnosis to recognising the importance of a local substernal continual aching pain a tympanitic aortic second sound and slight dilatation of the ascending aorta in cases already known to have late syphilis It is pointed out however that the interpretation of such signs in patients who are *not* known to have late syphilis is another matter and their true value can only be judged properly under such circumstances

Whilst the clinical features may be diagnostic of a syphilitic etiology the latter may be confirmed by a history of syphilis, signs of syphilis in other systems (particularly neurosyphilis) a positive Wassermann or Kahn reaction in the blood in about 85 per cent of cases a positive treponema pallidum immobilisation test (Nelson and Mayer 1949 Friedman and Olansky 1955) and a persistently raised erythrocyte sedimentation rate

Congenital syphilis does not cause aortitis (McCulloch 1930) although

spirochætes may be present in the aorta there is practically no tissue reaction

*Pathology* The initial lesion occurs in the adventitia and consists of syphilitic endarteritis of the vasa vasorum and of focal granulomatous tissue Although the inflammation spreads deeply into the media atrophy and necrosis of muscular and elastic fibres are partly due to ischæmia The damage is patchy and is repaired by fibrous tissue, the cross section of the aortic wall being correspondingly thinned at such points These medial scars are indicated on the inner surface of the vessel by depressions of the intima which presents a pock marked appearance Secondary atherosclerosis and extensive calcification are common

## ANEURYSM

*Sooner or later the diseased media may yield to the force of the blood pressure either generally or at its weakest point and a fusiform or saccular aneurysm results A fusiform aneurysm is little more than an exaggeration of the inevitable dilatation of a syphilitic aorta and has no greater consequences It is usually associated with aortic incompetence but may be seen radiologically when still uncomplicated (Rich and Webster, 1952) it then affords acceptable clinical evidence of relatively early syphilitic aortitis The diagnosis should be confirmed by a history of syphilis or by positive serological tests however for fusiform aneurysm may result from congenital hypoplasia of the ascending aorta or from non specific medial necrosis with or without dissection and slight dilatation of the aorta may be due to atherosclerosis and hypertension A ringing or amphoric second heart sound at the base of the heart may denote dilatation of the ascending aorta but does not indicate its cause Again a suspicious aortic second sound must be disregarded if the ascending aorta is seen to be normal in size and shape Irregularities in the calibre of the ascending aorta or aortic arch which may be clearly demonstrated by means of angiocardiography and calcification of the ascending aorta provide good evidence of syphilitic aortitis*

The syphilitic aneurysm proper is saccular (fig 14 01) and may occur in any part of the thoracic aorta particularly in the arch Aneurysm of the abdominal aorta is relatively rare and is less frequently due to syphilis Thus Mills and Horton (1938) attributed only 8 8 per cent of 80 abdominal aneurysms to syphilis and Estes (1950) only 5 per cent of 102 cases on the other hand Scott (1944) stated that syphilis was the cause of 58 per cent of his 96 cases The selective influence of specialised clinics no doubt explains the discrepancy

The M, F sex ratio in cases of saccular aneurysm is 10 1 (White 1937) partly perhaps because the aorta tends to be subjected to greater physical stresses in men than in women It is significant that saccular aneurysm rarely develops when there is aortic incompetence occurring in little over 10 per cent of such cases (Welty 1939) and that symptoms due to pressure

from an aneurysm may be relieved by an artificial arterio venous shunt conditions which reduce the mean aortic pressure

## *ANEURYSM OF THE ASCENDING AORTA*

Aneurysm of the ascending aorta may cause visible pulsation or a conspicuous pulsating tumour to the right or left of the sternum or in the suprasternal notch Symptoms may be absent or there may be sternal or costal pain from pressure erosion Pulsation may be expansile and may be accompanied by a systolic thrill On auscultation a loud systolic bruit is usually heard When invisible an anterior aneurysm may yet be detected by percussing a band of parasternal dullness More often it is first discovered radiologically (fig 14 01)



Fig 14 01—Saccular aneurysm of the ascending aorta



Fig 14 02—Angiocardiogram showing partial superior vena cava obstruction due to an aneurysm

*(By cour y f D F nc Ga dner)*

Partial obstruction of the superior vena cava is a not uncommon complication and gives rise to a high venous pressure in the head and neck while the right atrial pressure remains normal The distended jugular veins continue to pulsate as long as the obstruction is incomplete but if the venous pressure is very high pulsation may only be detected when the patient stands up A visible collateral venous circulation does not necessarily develop presumably because the block is incomplete so that a fair blood flow is maintained under the high head of pressure Puffiness or

œdema of the head and upper extremeties may occur, but in one case of the author's œdema was confined to the legs in the erect posture This was proved not to be due to anæmia chronic nephritis bilateral phlebothrombosis Milroy's disease low blood proteins thiamine deficiency or heart failure According to Katz (1954) chronic obstruction of the superior vena cava may result in salt and water retention by the kidneys in animals the mechanism is unknown The diagnosis of partial S V C obstruction may be proved by means of angiocardiography (fig 14 02) or by passing a venous catheter and noting the sudden fall in pressure as the tip slips through the obstruction

Aneurysm of the ascending aorta may rupture into the pericardial or pleural cavities into the pulmonary artery or into the right atrium

## *ANEURYSM OF THE ARCH*

The symptoms and signs of an aneurysm in this situation are determined by pressure on surrounding structures Practically any structure in or close to the superior mediastinum may be compressed according to the size and position of the aneurysm Thus pressure on one or other subclavian artery may lead to significant differences in the pulse and blood pressure in the two arms a rare complication of this is clubbing of the fingers on the affected side Pressure on the left bronchus causes collapse of the left lung which may be complete or partial the upper lobe being involved more often than the lower Inflammatory changes may occur distal to the obstruction particularly bronchiectasis The left bronchus may be depressed with each pulsation of the aneurysm the resulting downward pull on the trachea during systole may be readily detected at the cricoid cartilage and is known as a tracheal tug It is best elicited by standing behind the patient who should be seated and applying steady upward pressure on the cricoid cartilage with the tip of one forefinger Pressure on the trachea itself may give rise to an irritating cough to stridor or to considerable respiratory obstruction pressure on the left recurrent laryngeal nerve to a brassy cough and paralysis of the left vocal chord pressure on the œsophagus to dysphagia The phrenic nerve usually escapes as it lies superficially but the left sympathetic chain may be compressed with the production of Horner's syndrome (homolateral contraction of the pupil and drooping of the upper eyelid) Severe radiating pains may be caused by pressure on nerve roots and the spine may be eroded

## *ANEURYSM OF THE ABDOMINAL AORTA*

Of 1 459 aneurysms of the aorta collected from the literature by Unger and Poppel (1936) only 136 or less than 10 per cent were below the diaphragm and, as previously stated only about one in ten of abdominal aneurysms are syphilitic

An abdominal aneurysm usually presents as a pulsating tumour in the epigastrium over which a systolic thrill and murmur may sometimes be



(a) Anterior vi w



(b) Second oblique position

Fig 14 03—Skiagram showing several aneurysms of the aortic arch

(*By* *ou t sy f S J h Park nso* )



(a) Anterior view



(b) Lateral view

Fig 14 04—Calcified aneurysm of th aorta

detected Root pain associated with vertebral erosion is not uncommon or pain may be local A relatively common clinical error is to mistake a normal aorta projected forwards by lordosis in thin subjects for an aneurysm.

## RADIOLOGICAL DIAGNOSIS



Fig 14 05 —Skiagram showing erosion of the bodies of several dorsal vertebræ as the result of pressure from an aneurysm

Although the existence and site of a syphilitic aneurysm may often be recognised clinically their accurate diagnosis is essentially radiological Aneurysm may be distinguished from other rounded shadows in the vicinity of the aorta by four characteristic features (1) it is intimately connected with the aorta (fig 14 03) (2) it becomes opaque with the aorta in angiocardiograms (3) it pulsates unless it is thrombosed (4) some part of its wall may be calcified (fig 14 04) Erosion of the bodies of several vertebræ (fig 14 05) and compression of the trachea bronchus or œsophagus may sometimes be seen Confusion may arise however when a mediastinal tumour exhibits transmitted pulsation Tomography and if necessary angiocardiography are advised in all doubtful cases

## DIFFERENTIAL DIAGNOSIS

The chief problem is to distinguish aortic aneurysm from other space filling lesions in the mediastinum these include dermoid cyst lymphatic cyst thymic tumour intrathoracic goitre bronchial carcinoma and cold abscess of the spine In the author s experience all these have caused confusion whereas mediastinal adenopathy has not

*Dermoid cysts* are solitary anterior and present to one or other side of the mid-line they are rounded homogenous and sometimes calcified (fig 14 06) Solid teratomata are often irregular in outline and density and may contain teeth or bone

*Lymphatic cysts* are more posterior and may be single or multiple geographically they may be closely related to either the ascending or

descending aorta In the anterior skiagram they usually project either to the right of the ascending aorta or to the left in the region of the pulmonary artery or left atrial appendix (fig 14 07) In the latter position they may compress the pulmonary artery and cause physiological stenosis with all

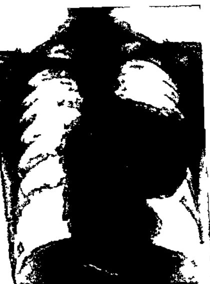


Fig 14 06—Calcified d rmo d cyst proved at post mortem
*(By cou tesy f S J h Park )*



Fig 14 07—Lymphatic cysts (proved by re section)

the characteristic physical signs and catheter findings In the case illus trated in figure 14 08, for instance in which there was a typical pulmonary systolic thrill and murmur the right ventricular pressure was 70/3 mm Hg and the pulmonary artery pressure beyond the point of compression 18,12 mm Hg when the cardiac output was 8 L/min )

*Thymic tumours or cysts* are also anterior and often malignant I have seen two calcified thymic cysts of many years duration both of which finally became malignant and invaded the pericardium and myocardium In anterior skiagrams the cyst or tumour presented to the left of the mid line just below the aortic knuckle (fig 14 09a) and in lateral views was seen to be well anterior (fig 14 09b) Pericardial pain effusion atrial flutter or fibrillation and characteristic electrocardiographic changes developed in both instances

*Retrosternal goitre* is easily recognised if it moves upwards on swallowing but may be mistaken for aneurysm if malignant and fixed

*Bronchial carcinoma* with secondary invasion of mediastinal glands and partial obstruction of the superior vena cava may sometimes be mistaken for aneurysm

*Tuberculous cold abscess* secondary to Pott s disease of the dorsal spi



(a) Anterior view



(b) Angiocardiogram of pulmonary artery



(c) Angiocardiogram of aorta



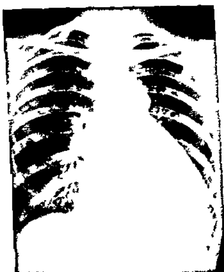

(d) The cyst after removal

Fig 14 08—Lymphatic cyst compressing the pulmonary artery

may sometimes be identified by its irregular ramifications especially when old and calcified In its active stage however it may present as a fusiform swelling behind the heart and may be mistaken for a syphylitic or dissecting aneurysm of the descending aorta

*Tomography* and *angiocardiography* have proved of great value in distinguishing aortic aneurysm from these and other mediastinal masses

*Retrograde aortography* is rarely necessary and in cases of syphilitic aortitis is probably dangerous



(a) Anterior view enlargement of the heart shadow is due to pericardial effusion



(b) Second oblique view showing the anterior superior position of the tumour

Fig 14 09—Calcified cystic malignant tumour of the thymus invading the pericardium and myocardium

The differential diagnosis between syphilitic and other forms of fusiform dilatation of the aorta is considered later in relation to aortic incompetence

## *COURSE*

Many aneurysms remain silent and are discovered accidentally by radiography others cause much suffering One of the worst features is the severe pain produced by pressure on bone especially the root pain associated with vertebral erosion This may last for months and be very resistant to treatment

The prognosis varies greatly but the average duration of life is little more than eighteen months from the onset of symptoms (Colt 1926–27) Cases have been reported however which have survived for fifteen to thirty years (Kauntze 1947) The chief dangers are infection of the lungs distal to bronchial compression and rupture Aortic aneurysm may rup

ture into the pericardium the pulmonary artery, the trachea or bronchus the œsophagus or the pleura giving rise to hæmopericardium with cardiac compression acute right ventricular failure with signs and symptoms of an aorto pulmonary shunt, dramatic hæmoptysis hæmatemesis or hæmothorax respectively usually with fatal results

## SPECIAL TREATMENT

The object of treatment apart from anti syphilitic measures is to promote thrombosis and calcification in the aneurysmal sac or to protect it by means of external fibrosis in order to prevent rupture or further expansion

Bed rest is necessary at first while routine anti syphilitic treatment is given During this period a course of calcium lactate 10 grains (0 6 G) t d s with vitamin D may be added to promote calcification in the wall of the aneurysm

If pain is not relieved by these measures surgical interference may be considered The old operation of inserting a wire into the sac in order to induce thrombosis is unsatisfactory the risk is considerable and effective clotting cannot be guaranteed Babcock s operation—the creation of an arterio venous communication between the carotid and jugular vessel (Babcock 1926 1932)—reduces the mean aortic pressure and may relieve pain (Ranson 1947) A more promising surgical method is to wrap the aneurysm in polythene cellophane this causes an intense fibroblastic reaction which protects the sac from without prevents further expansion and relieves pain (Poppe 1948) Resection of the aneurysm and replacement by an aortic homograft may be feasible when the lesion is below the left subclavian artery (Debakey and Cooley 1953 Rob 1954)

## AORTIC INCOMPETENCE

*Pathology* Weakening of the mesaorta in the region of the aortic valve leads to dilatation of the aortic ring and to separation of the cusps at their commissures so that the valve becomes incompetent Granulomatous tissue may also drive a wedge between the junctions of the cusps (fig 14 10) The cusps themselves become rolled and thickened at their free margins and present a dwarfed stunted appearance There is no stenosis and calcification is absent unless there is much secondary atherosclerosis Owing to the site of the lesion which is necessarily at the root of the aorta the mouths of the coronary vessels are often partly occluded either by active granulation tissue or fibrotic scarring Ischæmic fibrosis of the myocardium results

*Incidence* Syphilis used to account for about one third of all cases of aortic valve disease and for about one half of those in subjects between the ages of 40 and 60 (Cowan and Ritchie 1935) Of Campbell s series of 300 cases of aortic valve disease syphilis was responsible for 19 per cent only half of his cases however had aortic incompetence alone and of these syphilis was the cause in 38 per cent (Campbell 1932) At the present time

syphilis is probably still the most common cause of pure aortic incompetence between the ages of 40 and 60 but its frequency is declining

The sex ratio in syphilitic aortic incompetence is about 3 1 in favour of men (Campbell 1932) and is thus less remarkable than in aneurysm



Fig 14 10—Active syphilitic aortitis in a man of 6 showing granulomatous thickening around the coronary orifices and between the commissures of the thickened aortic cusp

*Clinical features* Syphilitic aortic incompetence has all the features of aortic incompetence in general (page 564) and some special characteristics of its own Only the latter will be considered here

1 The history of symptoms or of the discovery of the lesion is relatively recent usually a matter of weeks or months and rarely more than a year or two

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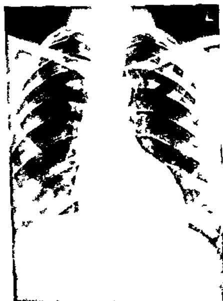


Fig 14 12—Syphilitic aortic incompetence the appearances here differ little from other forms of aortic valve disease



(a) Anterior view



(b) Second oblique position

Fig 14 13—Calcification of the ascending aorta in a case of syphilitic aortitis

*(By courtesy of Dr J S M C nn d Dr D C Porter)*

there is no stenosis no valve calcification no mitral valve disease and no rheumatic history Most syphilitic cases under the age of 30 are at first mistaken for rheumatic aortic incompetence especially because in these active granulomatous cases there is little if any dilatation of the ascending aorta or no more so than in any other type of free aortic incompetence A rheumatic etiology is favoured if the lesion is known to have been present for many years if there is no angina pectoris and if the sedimentation rate is normal

*Old dissecting aneurysm of the ascending aorta* involving the aortic valve and causing free incompetence is frequently mistaken for syphilitic aortitis even a fresh dissection with rapidly developing aortic incompetence may be confused with syphilis the new and severe valve lesion then being attributed to a ruptured cusp The dilated appearance of the ascending aorta and the free regurgitation lend credence to the error Occlusion of one or more of the great vessels arising from the arch of the aorta does not distinguish dissecting aneurysm from syphilitic aortitis—indeed the latter is the commonest cause of what has been termed reversed coarctation meaning normal femoral pulses and diminished or absent pulses in the subclavians and carotids This syndrome, also known as pulseless disease or Takayasu's disease is sometimes caused by a primary arteritis of the aortic arch especially when it occurs in young women (Ross and McKusick 1953) but in such case there is no aortic incompetence

Old dissecting aneurysm (q v ) should be suggested by the history the presence of hypertension the negative serology and the normal sedimentation rate

*Congenital hypoplasia of the ascending aorta* (q v ) may cause conspicuous dilatation of the aorta from the valve ring to the origin of the innominate artery with free aortic incompetence Associated arachnodactyly some other congenital anomaly or the long history may at once suggest the correct diagnosis

*Bacterial aortic endocarditis* active or old is sometimes confused with syphilitic aortitis Aneurysm of an aortic sinus perforation of a cusp free aortic incompetence high sedimentation rate and the development of severe heart failure towards the end of penicillin treatment are common to both diseases If the fever is low grade blood culture negative and W R doubtful the differential diagnosis may be very difficult in the absence of other pathognomic signs of bacterial endocarditis

*Atherosclerotic aortic incompetence* is suggested by the age of the patient some evidence of stenosis calcium in the aortic knuckle but not in the ascending aorta, and valve calcification Angina pectoris is common owing to the frequency of associated coronary disease but the sedimentation rate is normal and serology negative

*Course* The prognosis is bad the average duration of life being about two years (Campbell 1932) Left ventricular failure develops sooner or later in many cases, and congestive heart failure follows The downhill

course differs from that of other forms of aortic incompetence in its rapidity in the frequency of angina pectoris and in the relatively high proportion of sudden deaths (Munck 1946)

A rather more hopeful outlook is given by Webster *et al* (1953) who were able to trace 75 per cent of 1 020 cases seen over a period of twenty years at the Johns Hopkins Hospital 51 per cent of those that were initially symptom free survived ten years when angina pectoris was present 28 per cent survived ten years, when congestive failure was present only 6 per cent so survived

## ANGINA PECTORIS

*Pathology* It is often said that aortic valve disease may cause angina pectoris Whilst this is true the statement needs amplification Angina is a common complication of all forms of aortic stenosis and of *syphilitic* aortic incompetence but not of other varieties Rheumatic aortic incompetence for example must be gross to cause angina and rarely does so The explanation is to be found in the physiology of the coronary circulation During systole ventricular contraction prevents blood flowing through coronary vessels which penetrate left ventricular muscle and large arteries on the surface dilate to form an elastic reservoir which in recoil during diastole acts as an accessory pump forcing the blood onwards The higher the systolic pressure the greater the elastic reservoir provided the coronary arteries are healthy During ventricular relaxation blood is able to flow through vessels penetrating muscle being propelled by the aortic diastolic pressure and by the recoil of the elastic reservoir just mentioned Thus the coronary flow depends upon both systolic and diastolic pressures i e upon the mean pressure

Now in aortic stenosis the mean blood pressure is often low but in aortic incompetence although the diastolic pressure may be 40 or 50 mm of mercury the systolic pressure is commonly raised and the mean pressure adequate Syphilitic aortic incompetence causes angina pectoris because there is associated stenosis of the mouths of the coronary arteries if syphilitic aortitis produces sufficient damage in the region of the aortic cusps to cause aortic incompetence it is unusual for the mouths of the coronary vessels to remain unscathed Conversely if the mouths of the coronary vessels are so stenosed as to cause angina pectoris it is practically impossible for the root of the aorta to remain healthy Thus syphilitic angina is rare without aortic incompetence

*Clinical features* Syphilitic angina has certain characteristics which help to distinguish it from other types (1) the attacks tend to be of longer duration (2) they are more often nocturnal although the ordinary relationship to effort holds good (3) they are less often relieved by trinitrin Coronary thrombosis is a rare complication because ischæmia is due to stenosis of the coronary ostia and not to changes in the coronary vessels themselves Myocardial infarction however may occur without coronary thrombosis,

especially when the effect of gross occlusion of the mouths of the coronary vessels is exaggerated by a drop in blood pressure from some other cause, such as surgical shock Ischæmia of the least nourished part of the myocardium may then be so pronounced as to cause necrosis even so cardiac infarction in uncommon Of 58 cases of sudden death from syphilitic aortitis studied by Munck (1946), for instance only four had a myocardial infarct

*Course* The prognosis is poor 75 per cent of patients living less than ten years (Webster *et al* 1953) Statu anginosus may develop before the end or nocturnal angina may prove troublesome When heart failure develops angina may disappear it is not clear why this should be so, but it may depend upon changes in tissue metabolism.

*Special treatment* The ordinary methods of treating angina pectoris are applicable to the syphilitic type although the results are poor Anti syphilitic measures should not be withheld Bed rest is particularly important during the first six weeks of treatment and is essential during the first course of penicillin (or arsenic) In relatively young subjects with granulomatous obstruction of the coronary ostia remarkably good results may be achieved with penicillin

## HEART BLOCK

True syphilitic heart block is very rare and depends upon interruption of the bundle of His by gummatous tissue On the other hand heart block resulting from interference with the conducting tissue by ischæmic fibrosis due to stenosis of the coronary ostia is not uncommon and like angina pectoris and for the same reason is nearly always associated with aortic incompetence The former may respond to iodine or penicillin therapy the latter of course does not

## SPECIFIC TREATMENT OF SYPHILITIC AORTITIS

Syphilitic aortitis should be fully treated with anti syphilitic drugs whether uncomplicated or otherwise Clearly past damage cannot be repaired but active granulomatous tissue can be abolished and further activity prevented

*The patient should be put to bed for four weeks* and during the first three weeks should receive potassium iodide 10 grains (0 6 G) t d s preferably with liq hydrarg perchlor 60 minims (4 ml) Gummatous tissue resolves with this treatment and the danger of a severe Herxheimer reaction is lessened After two to three weeks of such treatment 1·2 million units of procaine penicillin are given over a period of 10 days in divided doses of 600 000 units twice daily Alternatively a single daily injection of 600 000 units of penicillin may be given over a period of three weeks Reactions are rare (Moore 1947)

Shortly after completing the penicillin course the patient may be allowed up and treatment with bismuth begun Intramuscular injections of 0 1 G

of bimostab weekly for six weeks followed by 0 2 G weekly for the next six weeks are advised Some prefer to start treatment with bismuth and dispense with iodine and mercury altogether Others use penicillin alone In view of its more toxic nature arsenic has now been abandoned in the treatment of cardiovascular syphilis being superseded by penicillin

The development or aggravation of angina pectoris or heart failure are major dangers but both are unlikely and when they do occur cannot always be attributed to the treatment

Herxheimer reactions are not prevented by starting with small doses of penicillin but are inhibited by preliminary iodine mercury or bismuth The occasional development of heart failure following penicillin treatment is attributed to an increase in the degree of aortic incompetence as con tracting scar tissue replaces granulomatous inflammation A rather similar situation is common in bacterial endocarditis

The regime described constitutes one complete course of treatment and lasts four months The situation should then be reviewed particular atten tion being paid to the E S R If this is normal treatment may be discon tinued but if still raised, a second course of penicillin is advised Bed rest is no longer necessary unless congestive failure, angina pectoris or some other complication demands it Since there is now no danger of a Herx heimer reaction there is no need to repeat iodine mercury or bismuth

A third or fourth course of penicillin should be given without hesitation if there is any further evidence of activity

It is repeated for emphasis that neither aneurysm angina pectoris nor heart failure contraindicates penicillin for the Herxheimer reaction is rare This phenomenon consists of a local tissue reaction which may cause swelling and occlusion of the coronary ostia with disastrous results

Statistics have shown that the effect of full anti syphilitic measures before the introduction of penicillin was to improve the average life expectancy from eighteen months to two years (Padget and Moore 1935) It may be argued that the increased care and enforced rest which are a necessary corollary to this form of treatment might also improve the prognosis by a similar amount and there is something to be said for the view that there is little point in attempting to extirpate the spirochæte once heart failure or angina pectoris has developed for it is then probably too late However the great majority of untreated cases show active syphilitic aortitis at necropsy whereas treated cases do not (Webster and Reader 1948) and there are a sufficient number of cases that benefit from subsidence of this active inflammation to make routine treatment well worth while

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CHAPTER XV

# ISCHÆMIC HEART DISEASE

## DEFINITION

OCCLUSIVE disease of the coronary arteries of sufficient degree to prevent the coronary circulation meeting the physiological demands of the heart is best described as ischæmic heart disease It is characterised clinically by angina pectoris acute coronary insufficiency, and cardiac infarction pathologically by occlusive coronary atherosclerosis with or without thrombosis, and by focal or massive ischæmic myocardial necrosis and fibrosis

## INCIDENCE

Occlusive coronary atherosclerosis is responsible for about 30 per cent of all cases of organic heart disease and for about 80 per cent of all sudden cardiac deaths (Munck 1946) moreover it appears to be increasing rapidly thus the number of cases dying from coronary disease in England per million persons living was 48 in 1926, 148 in 1930, 473 in 1939 (Cassidy 1946) and 1 392 in 1953 (Registrar General s review) The increasing age of the population is no doubt partly responsible thus the citizens of ancient Rome in their halcyon days had an average life span of twenty to thirty years and the following table shows the increased average life span in the U S A from 1879 to 1944 (Master 1947)

| | |
|---|---|
| 1879–1899 | 34 years |
| 1911–1912 | 46 63 years |
| 1919–1920 | 51 14 years |
| 1930 | 57 36 years |
| 1944 | 64 40 years |

These remarkable figures are chiefly due to the successful war against infections and parasitic diseases and to the saving of life by surgical means Another factor that must be taken into account is the attitude of medical practitioners who in 19_6 had scarcely heard of coronary thrombosis whereas now they are apt to diagnose it more frequently than it exists It should be remembered that coronary thrombosis was not recognised as a clinical entity until its classic description by Herrick in 1912 despite Leyden s lucid account in 1884 and was not widely appreciated in Great Britain until popularised by McNee in 1925 and Gibson (1925)

*Sex* Of Heberden s 100 cases of angina only three were women (Heberden 1802) Most investigators give the general sex ratio as 4 1 in favour of men but under the age of 50 it is 8 1 (Hedley 1939) and under the

age of 40 male predominance is overwhelming in fact, angina in women under 40 is nearly always due to some other etiological agent such as hypertension aortic stenosis syphilitic aortitis anæmia, myxœdema diabetes mellitus xanthomatosis or paroxysmal rhythm change Between the ages of 60 and 70, however about one third of the cases are women and over the age of 70 the sex incidence is equal (Gordon Bland and White 1939)

*Age* Of 1 000 cases seen personally by Cassidy (1946) 70 per cent were between 50 and 70 years of age of the men 14 6 per cent were between 40 and 50 3 2 per cent between 30 and 40, and 0 25 per cent were under 30 These figures are in harmony with common experience except perhaps with regard to the incidence in young men, for many such cases were seen in the Services during the second world war (Newman 1946 Poe 1947) The peak age of death is 60 (Hedley 1939)

*Hereditary factor* A familial incidence of coronary disease was found in 50 per cent of Cassidy s 1 000 cases and was four times as common in Yater's 744 young cases (under 40) as in normal controls (Cassidy, 1946 Yater *et al* 1948)

*Habits and occupation* There is a general impression that the incidence of ischæmic heart disease is particularly high amongst professional men and is related to the stress of modern urban life There is said to be little to support this view (Master 1947) but some figures published by Hedley (1939) are interesting

| *Occupation* | *Deaths from coronary occlusion per* 100,000 |
|---|---|
| Professional | 154 |
| Managers and officials | 140 |
| Clerks and salesmen | 128 |
| Skilled and unskilled workers | 107 |

The author however ascribed the difference in these figures to more accurate certification in those earning larger incomes

Nevertheless the obstinate belief that angina pectoris is a doctor s disease persists and appears to be justified by startling figures published by Ryle and Russell (1949) These workers who were especially well qualified to sift and present evidence of the kind required divided the social strata of England and Wales into five classes and found that the standardised mortality ratio (S M R ) from ischæmic heart disease in social class I (professional workers) was twice that in social class III (skilled artisans) and three times that in class V (unskilled workers) Their table giving the actual occupations with the four highest and four lowest standard mortality ratios ends the debate on this previously vexed question and once again emphasises the fact that experienced opinion should not be too readily cast aside because of ill founded statistical evidence to the contrary Physicians and surgeons head the list with an S M R of 368 proprietors of wholesale business came second with an S M R of 235 the legal profession third

(227) and the Church fourth (218) At the other extreme we have workers in chemical processes with an S M R of only 20 agricultural labourers 32 stone miners and quarriers 38 and coal miners engaged in other work 40 More recently Morris *et al* (1952) showed that ischæmic heart disease was twice as common in general practitioners as in consultants or specialists

It is by no means clear what factors are responsible for the higher incidence of ischæmic heart disease in certain occupations and social classes the degree of mental stress and strain or other psychological factor the type of diet or standard of nutrition and the amount of day to day physical inactivity have each been suspected but as yet there is little convincing evidence favouring one more than another Morris *et al* (1953) however have brought forward interesting data which they thought might implicate physical inactivity They found for instance that conductors on double decker buses and postmen were less likely to develop ischæmic heart disease than bus drivers executive officers telephonists and post office clerks

There is no evidence that alcohol (Wilens 1947) is responsible for the high male incidence or has any permanent influence on the course of the disease Cassidy (1946) exonerated smoking but recent statistical studies have shown that ischæmic heart disease is about one and a half times more common in cigarette smokers than in non smokers (Doll and Hill 1954 Hammond and Horn 1954)

## PATHOGENESIS

Ischæmic heart disease is due to occlusive coronary atherosclerosis with or without secondary subintimal hæmorrhage or thrombosis Angina pectoris caused by *syphilitic aortitis* aortic stenosis severe anæmia paroxysmal tachycardia and the like and coronary occlusion resulting from angiitis *embolism trauma* dissecting aneurysm and other rarities are considered elsewhere

The cause of human atheroma remains unknown despite a great deal of work on the subject (Cowdry 1933 Katz and Stamler 1953) The word atheroma comes from the Greek ἀθήρη meaning groats i e crushed corn or gruel (American mush) and ὦμα a swelling Lipoid substances accumulate in the intima of the aorta and larger arteries in a patchy irregular fashion causing a variable degree of pressure atrophy of the underlying media and sometimes *encroaching* on the lumen of the vessel (fig 15 01) The degree of narrowing of an atherosclerotic coronary artery cannot be accurately assessed by its appearance at necropsy, for in life the blood pressure tends to iron out the excrescences and maintain a smooth intimal surface and full lumen (*Harrison* and Wood 1949) Indeed Duguid and Robertson (1955) maintain that an atherosclerotic vessel *per se* is dilated and that narrowing of the lumen is only caused by thrombosis

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Hunter (1796) Erosion or ulceration of atheromatous lesions forms an excellent nidus for secondary thrombosis This is the common cause of acute coronary obstruction Organisation of such thrombi leads to micro copical appearances similar to atherosclerotic lesions indeed it has been

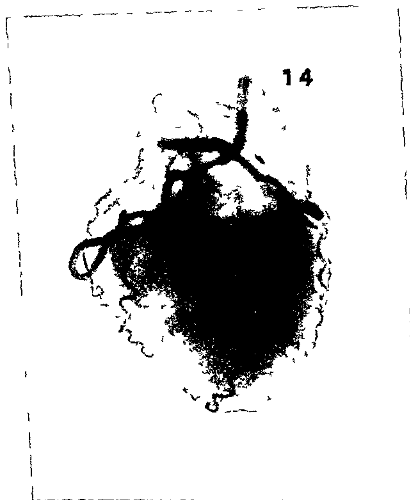



Fig 15 01 (b)—Normal control for comparison

suggested that atheroma may represent nothing more than intravascular clotting (Duguid, 1946 1948)

*Etiology of atherosclerosis*

As a result of a vast amount of work on this important subject the sterile doctrine that atherosclerosis is an inevitable consequence of growing old has been largely abandoned instead it is now believed that atherosclerosis

is closely related to disturbances of fat metabolism usually acting over a long period of time (Katz and Stamler 1953) and perhaps also to some alteration in the biophysical properties or biochemical structure of the intima itself (Page 1954) The evidence upon which these conclusions are based can be summarised only very briefly here, but before doing so it may be helpful to digress for a moment on the nature of the blood lipids

*The blood lipids*

Fatty substances in normal blood include neutral fat fatty acids free cholesterol cholesterol esters and phospholipids

Following a fatty meal the plasma may become opalescent this is due to the transport of neutral fat and fatty acids combined with protein in the physical form of chylomicrons which are microscopically visible fatty bodies less than 1μ in diameter Moreton s view that these bodies might play an etiological role in atherosclerosis (Moreton 1948) has not been shared by subsequent workers (Gofman *et al* 1950) Chylomicrons contain less than 5 per cent of cholesterol have very high $S_f$ values around 40 000 units (*vide infra*) and change their structure after an injection of heparin when they develop $S_f$ values under 10 (Graham *et al* 1951)

Cholesterol and phospholipids also of course insoluble in water are carried in combination with $\alpha$ and $\beta$ globulins as $\alpha$ and $\beta$ lipoproteins which are microscopically invisible macromolecules of various sizes and densities The total serum cholesterol which is normally around 150 to 300 mg per cent, is certainly related to atherosclerosis but has been found to be only a crude measure of blood lipid disturbance

Gertler *et al* (1950) emphasised the part played by the cholesterol esters and the *phospholipids* and suggested that the cholesterol/phospholipid ratio was more closely related to atherosclerosis than the total serum cholesterol This ratio is normally about 0 85 to 1 0 (Barr 1953) the amount of phospholipid tending to be proportional to the amount of free cholesterol present rather than to the quantity of cholesterol esters Ratios above unity mean that the cholesterol esters have risen more than the free cholesterol High ratios are found in all diseases known to encourage atherosclerosis

Such measurements however give no information about the biophysical properties of the macromolecules in which these substances are incorporated The lipoproteins however may be fractionated biochemically (Cohn *et al* 1946) or by means of electrophoresis (Pearsall and Chanutin 1949) or the ultracentrifuge (Gofman *et al* 1950) Russ Eden and Barr (1951) found that practically all the serum cholesterol was incorporated in Cohn s fractions A and C, i e in the $\alpha_1$ and $\beta_1$ lipoproteins 30 per cent in the former and 70 per cent in the latter They also found that the cholesterol/phospholipid ratio was about 0 5 for the $\alpha_1$ lipoproteins and 1 35 for the $\beta_1$ lipoproteins (If phospholipids are expressed in terms of phosphorus these ratios should be multiplied by 25) In atherosclerosis

and diseases known to encourage it, there is a relative and usually absolute increase in the $\beta_1$ lipoproteins even when the total blood cholesterol is normal and the cholesterol/phospholipid ratio less than unity (Barr, Russ and Eden 1951 Oliver and Boyd 1955)

In the hands of Gofman and his associates (1950) the ultracentrifuge proved a useful tool for separating lipoproteins of different densities The density of the macromolecules believed to be most closely related to atherosclerosis is close to 1 G /cc If the density of the solution containing them is adjusted to 1 063 by means of sodium chloride they will float with varying degrees of facility according to their densities The $a_1$ lipoproteins being denser than the solution will not float and are therefore immediately separated out In the Svedberg ultracentrifuge molecules that sediment at a rate of $5 \times 10^{13}$ cm per second per unit field of force are said to have a value of 5 S (Svedberg) units For flotation rates the same Svedberg unit is used with the suffix f Thus molecules that float at rates of $20 \times 10^{13}$ cm per second per unit field of force are said to have an $S_f$ value of 20 It will be understood therefore that the higher the $S_f$ value the lighter the molecule. Using this technique Gofman *et al* (1950) have divided the lipoproteins into classes according to their flotation rates. Those not analysed being denser than 1 063 (the arbitrary density of the solution) are the $a_1$ lipoproteins which do not seem to be closely correlated with atherosclerosis Of the large $\beta_1$ lipoprotein fraction the chief $S_f$ classes are 2 to 10 12 to 20, 20 to 35 (35 to 100) and 100 to 40 000 The lipoproteins shown to be closely related to atherogenesis are those with $S_f$ values of 12 to 20 and 35 to 100 (Gofman *et al* 1952)

*Evidence that atherosclerosis is related to altered blood lipids*

The chief evidence supporting the view that atherosclerosis and ischæmic heart disease are related to disturbances of blood lipid transport or meta bolism may now be summarised

1 In the animal kingdom man alone suffers commonly from athero sclerotic disease the total blood cholesterol cholesterol esters cholesterol/ phospholipid ratio $\beta_1$ lipoproteins and the concentration of lipoprotein macromolecules of the $S_f$ 10–20 and 35–100 class are all considerably higher in man than in any other mammal (Barr 1953)

2 Only the new born normal infant is immune from atherosclerosis children young adults and women during the child bearing age are relatively immune the frequency of atherosclerosis in men increases with age at least up to the end of the sixth decade The blood concentration of the particular classes of lipoprotein mentioned above is relatively low in the more or less immune groups but relatively high and increases with age in susceptible men (Gofman *et al* 1950)

3 Œstrogens tend to restore the normal blood lipid pattern (Barr 1953) androgens have the reverse effect (Russ *et al* 1955) Atherosclerosis increases after bilateral oophorectomy in women (Wuest Dry and

Edwards 1953) By the age of 70 the M/F sex ratio in ischæmic heart disease is unity

4 All diseases known to be associated with the altered blood lipid pattern described above are also associated with a high incidence of severe atherosclerosis these diseases include diabetes mellitus, myxœdema xanthomatosis nephrosis and familial hypercholesterolæmia (Gofman *et al* 1951 Katz and Stamler 1953) The same abnormal blood lipid pattern is the rule in spontaneous ischæmic heart disease

5 Atherosclerosis has been produced experimentally in animals only by means of a high cholesterol intake first in rabbits (Anitschkow, 1913 Leary 1934) then in chicks (Dauber and Katz 1942) dogs with the aid of thiouracil (Steiner Kendall and Bevans 1949) hamsters (Goldman and Pollack 1949) and guinea pigs (Altschul, 1950) Experimental atherosclerosis in omnivorous animals has the same distribution as in man

6 The atheromatous lesions themselves contain a high proportion of cholesterol (Windaus 1910) as has been known for a century (Cowdry 1933)

7 Atherosclerosis is rare in people who live on a vegetarian diet low in fat (Steiner 1946) and the incidence of clinical diseases due to atherosclerosis fell sharply in Northern Europe during the second world war parallel to the decline in the consumption of foods rich in cholesterol (Malmros 1950) According to Wilens (1947) severe atherosclerosis is ten times as common in obese subjects as in the lean Keys (1952) emphasized the importance of total fat intake rather than cholesterol intake per se Gofman and Jones (1952) have shown that obese subjects tend to have a higher concentration of lipoprotein of the $S_f$ 35–100 class than lean subjects, there was less relationship however between obesity and lipoproteins of the $S_f$ 12–20 class Gofman *et al* (1950 1951) have also shown that prolonged low fat diets gradually reduce the blood concentration of the abnormal lipids

*The part played by the intima*

While it is now generally agreed that abnormal blood lipids are an important factor in the production of atherosclerosis it is far from clear just how they operate

Wilens (1951) showed that serum could filter through an artery from the lumen outwards Experimentally the filtrate was unchanged serum in respect of most inorganic substances but contained very little cholesterol relatively little protein and a diminished amount of calcium these substances becoming highly concentrated in the serum within the vessel The rate of filtration was proportional to the filtration pressure i e to the blood pressure, Some of the cholesterol penetrated the intima but its further progress was barred by the internal elastic lamina

The filtration theory of atherogenesis (Page 1954) is based on observa-

tions of this kind and implies that cholesterol deposits may accumulate gradually over the years in normal individuals but that they may do so much more rapidly and in far greater degree in the presence of raised blood lipoproteins of the kind best adapted to penetrating the intima especially if the filtration pressure is high (as in hypertension) and if there are changes in the ground substance of the intima increasing its permeability

The presence of abnormal lipoproteins with particular biophysical properties has certainly been demonstrated in atherosclerosis but whether these are best adapted to penetrate the intima and be prevented from passing through the internal elastic lamina is as yet unknown Certainly also atherosclerosis is twice as frequent in hypertensive subjects as in those with normal blood pressures (Wilens 1947) There is evidence that most atherosclerotic lesions are preceded by some change in the ground substance of the intima and by subendothelial fibroblastic proliferation (Moon and Rinehart 1952) A certain degree of protection against cholesterol induced atherosclerosis in rabbits and chicks is afforded by both potassium iodide and thyroid hormone whether the blood lipids are favourably influenced by these substances or not (Katz and Stamler 1953) it has been suggested that this favourable effect is due to the decreased permeability of the vascular endothelium which is known to follow the administration of these drugs

## ANGINA PECTORIS

*Physiology* Angina pectoris and its close relative the pain of intermittent claudication are believed to be due to certain metabolites that are formed in ischæmic working muscle (Lewis 1934) Whatever the precise explanation for the development of pain there can be no doubt that attacks depend upon relative myocardial ischæmia an idea first enunciated by Parry (1799) The term angina pectoris is customarily applied to transient pain only and refers to ischæmic attacks provoked by temporary stress during which the metabolic demands of the myocardium are beyond the capacity of the coronary circulation

Such a situation may arise during effort (1) if the coronary vessels are more or less occluded either at their mouths as in syphilitic aortitis or during their course as in atherosclerosis various forms of angiitis and embolism (2) if the coronary flow is diminished by other means such as aortic stenosis gross aortic incompetence tight mitral stenosis a high pulmonary vascular resistance or severe pulmonary stenosis (3) if the blood itself carries insufficient available oxygen as in anæmia or at high altitudes or (4) if the regular work of the heart is increased by such conditions as hypertension valve disease or hyperkinetic circulatory states

Although only angina pectoris resulting from coronary atherosclerosis concerns us here the other factors mentioned often play a contributory role thus anæmia may precipitate angina in a case of previously silent

coronary disease not only because of the limited oxygen transport, but also because the work of the heart is increased in order to maintain a high cardiac output. Hypertension is particularly important in so far as it increases the work of the heart and contributes to the development of atheroma on the other hand it tends to iron out the plaques and so may prevent coronary narrowing in fact most cases of hypertensive heart disease have dilated coronary arteries (Harrison and Wood 1949). Clinically although more than half of all cases of ischæmic heart disease have blood pressures above 160/100 mm Hg (Cassidy, 1946) systolic pressures over 200 mm Hg are rare (Riseman and Brown 1937)

## CLINICAL FEATURES

Angina is a symptom and must be distinguished from other pains in the upper half of the body by a careful analysis of its qualities and behaviour

*Site* The pain is central mid sternal and tends to radiate bilaterally across or round the chest into the sides of the neck and jaws or even into the face or nose into the shoulders and down the inner or outer sides of the arms sometimes as far as the little fingers or thumbs occasionally through to the back between the shoulder blades (fig 15 02) This full distribution was experienced by John Hunter (1796) It is not situated in the left inframammary area although it may be more left pectoral than sternal Radiation may be unilateral and it is true that the left side then suffers more often than *the right*, but it must not be thought that spread down the left arm is either especially typical or diagnostic for bilateral spread is more typical and many other pains may radiate down the left arm including left inframammary pain Although centrifugal spread is the rule radiation is occasionally centripetal the pain starting in the wrists upper arms or face and spreading thence to the chest Pain may even be confined to one of the points of radiation e g to the face back or wrist not being felt in the front of the chest at all

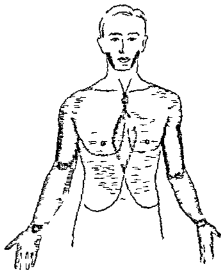


Fig 15 02—Diagram illustrating radiation of pain in ischæmic heart disease

*Character* Angina pectoris is classically constricting squeezing pressing or crushing, it is sometimes stinging numbing or burning sometimes it

cannot be described adequately by the patient It is not sharp shooting or stabbing which are the usual adjectives applied to left inframammary pain An important characteristic is its constancy the pain being steady while it lasts apart from initial waxing and final waning no pain which repeats itself in a succession of jabs or knife like thrusts is angina

*Duration* Attacks are measured in minutes usually they last two or three minutes occasionally five or ten they are not momentary, nor do they continue for hours and any pain that behaves in either of these ways is not angina pectoris (as defined above)

*Provocation* Angina is characteristically produced by any effort that increases the metabolic demands of the myocardium beyond the capacity of the coronary circulation and patients often know or learn the precise amount of effort necessary to provoke pain When the critical point is reached the patient usually feels compelled to stop whatever he is doing and to stand still until the pain passes off Attacks are brought on especially by walking uphill or against the wind by hurrying after meals by going out of a warm room into the cold or by any unaccustomed exercise less so by manual work to which the subject is trained Pain may also be induced by excitement anger fear or apprehension In advanced cases pain is provoked by lying down (angina decubitus) or stooping tending to occur when the patient first gets into bed at night or waking him from sleep It may then depend upon the rise in cardiac output that follows change of posture from vertical to horizontal or upon anxiety dreams

Pain that occurs after effort but not during it or that is provoked by lying on the left side or by the adoption of some particular posture (other than stooping or lying) is not angina these features are characteristic of left inframammary pain

The degree of angina pectoris (grade of effort intolerance) may be assessed according to the speed with which the patient is able to walk—not the distance In grade I pain is only provoked by hurrying or walking up hills or several flights of stairs in grade II walking on the level at an average speed causes pain usually within the first 300 yards in grade III pain occurs even when walking slowly and in grade IV there is pain at rest and total incapacity

As implied above patients with moderate angina usually complain of pain soon after the beginning of effort or not at all (Kemball Price 1951) if they do not have pain in the first quarter mile then can very likely walk indefinitely at the same speed Again if the pain is not severe patients can often walk it off This behaviour is presumably related to the effect of exercise on vasomotor tone i e to second wind

## *DIAGNOSIS OF ANGINA*

If a pain conforms in site quality duration and relation to cardiac work to the features mentioned above it is angina pectoris and the diagnosis

must stand under any conditions except malingering The diagnosis should stand likewise when pain conforms to the required features in three out of the four respects mentioned provided it is not untenable in the fourth For example if a constricting pain brought on only by exertion and lasting but two or three minutes is localised in the left inframammary area it is probably not angina for the site makes the diagnosis untenable even though it conforms in the other three respects On the other hand if the same pain is situated in the left pectoral region between breast and clavicl it is almost certainly angina because this site though atypical is not contradictory Again a midsternal pressing pain brought on only by effort but lasting fifteen minutes is probably angina for the long duration though unusual is not altogether conflicting but should it last two hours it is not angina as defined above

It is sometimes said that certain associated symptoms such as breathlessness dizziness or faintness flushing sweating weakness and a feeling of impending death help to confirm the diagnosis It cannot be stressed too strongly that these symptoms carry little weight, for they are vasomotor in origin and although they may be provoked by an attack of angina they are in no way characteristic of it and are much commoner in the anxiety states*

The differential diagnosis includes anxiety states functional disord or organic disease involving the dorsal spinal ligaments œsophageal or gastric spasm or distension diaphragmatic hernia and conditions causing respiratory distress

*Anxiety states* with left inframammary pain present no diagnostic difficulty but when pain is parasternal or even central it may be very confusing The patients are usually women near the menopause and they may describe a central pain radiating to the throat jaws and arms during or after effort when reaching up to a high shelf when washing or using their arms in other ways, and sometimes when emotionally upset As noted by Cassidy (1946) the attacks are apt to be widely spaced unrestricted effort causing no distress between them Complete investigations may reveal nothing significant in any system and the nature of the attacks remains obscure Angina can only be excluded and then with some uncertainty by obtaining a normal electrocardiogram during spontaneous or induced pain.

*Referred pain from the dorsal spinal ligaments* may be felt across the front of the chest as in the experimental work of Lewis and Kellgren (1939) Attacks may be related to posture or reproduced by spinal movements or pressure over the interspinous ligaments from D2 to D4

*Œsophageal spasm* may cause central chest pain radiating down both arms and tight or bursting in quality There is no close relationship to effort and bouts may be periodic like any other gut colic The diagnosis may be proved by demonstrating œsophageal spasm by means of fluoroscopy and by obtaining a normal electrocardiogram during attacks (Wolferth and Edeiken 1942)

*Diaphragmatic hernia* may cause pain on effort similar to angina pectoris but attacks also occur without provocation especially when the patient lies down and at times even strenuous effort may be symptom free Severe attacks may be mistaken for cardiac infarction The diagnosis is made by means of a barium meal fluoroscopy being carried out with the patient tilted head down (Dwyer, 1937)

Relief of pain by belching in any disorder of the œsophagus or stomach is less helpful in distinguishing such conditions from angina pectoris than might be supposed for ischæmic pain may be similarly relieved in about 10 per cent of cases (Riseman and Brown 1937) Pain after meals is also common in cases of angina pectoris although slight effort may be necessary to provoke it

*Bronchial asthma* or extreme dyspnœa from any cause may be associated with a feeling of substernal tightness that should not be confused with angina pectoris for breathlessness is not a feature of transient myocardial ischæmia

## PHYSICAL EXAMINATION

Having made the diagnosis on historical grounds the patient should be examined with a view to ascertaining the cause of the ischæmia Aortic valve disease and severe anæmia should be recognised by their characteristic features the presence of obesity or of hypertension noted the mental state of the patient assessed and attention should be paid to any other factor that may have a bearing on the frequency or severity of attacks In this respect, diabetes mellitus and polycythæmia must be borne in mind In the majority of cases however there are no physical signs the rhythm is normal the heart is not enlarged there are no murmurs and there is no evidence of congestive failure the peripheral and fundal arteries and the blood pressure may provide no evidence of general vascular disease fluoroscopy shows a heart shadow normal in size shape and pulsation and the electrocardiogram may be normal at rest It is repeated for emphasis that this apparent normality of the cardiovascular system is typical of pure angina pectoris due to coronary atherosclerosis and that with few exceptions physical signs radiological changes or electrocardiographic abnormalities are due to complications or associated disease even the demonstration of peripheral atherosclerosis proves little for it is common enough without serious involvement of the coronary vessels, and is often missing with advanced coronary disease

## SPECIAL TESTS

Most of the special tests are of little help for the circulation is usually normal at rest Effort tolerance tests based on the behaviour of the pulse rate and venous pressure are of no value Reproduction of pain by prescribed effort for purposes of accurate analysis is sometimes useful with a

bad witness or pain may be induced to ascertain the prophylactic or curative effect of trinitrin The only reliable test, however, is to obtain an electrocardiogram immediately after effort (Scherf and Goldhammer 1933) when characteristic depression of the RS T segment with or without inversion of the U wave clinches the diagnosis (fig 15 03) The depression should measure 1 mm or more below the level of the atrial T wave and should remain flat or slope downwards for at least 0 08 second A depressed RS T junction followed by an upwardly sloping RS T segment is normal The best method is to make the patient exercise until he is in pain if he stops on account of fatigue or breathlessness without developing pain angina is unlikely* In the author s experience (Wood *et al*, 1950) only 5 per cent of electrocardiograms remain normal during or immediately after an attack of true angina or after sufficient effort to cause breathlessness and fatigue (in ischæmic subjects)

This test is not entirely without danger and should only be carried out when the diagnosis is really in doubt and the resting electrocardiogram normal or equivocal

The other method is to take serial electrocardiograms while the patient breathes 10 per cent oxygen for twenty minutes or for a shorter time if pain is produced As depression of the RS T segment occurs in normal subjects with this test a positive result is only accepted if the depression exceeds 2 5 mm in any lead or if the T wave becomes inverted in left ventricular surface leads or their counterparts (Larsen 1938 Levy *et al* 1938 1939 1941) The test is positive in 3 to 5 per cent of normal control (Biorck 1946 Weintraub and Bishop 1947) in 15 to 20 per cent of cases of doubtful angina and in 50 to 55 per cent of cases of undisputed angina (Levy *et al* 1941 Biorck 1946) In the opinion of the writer this test is less useful than the effort test being more difficult to carry out more difficult to interpret more dangerous, and far less frequently positive The subject is well reviewed by Stewart and Carr (1954)

## COURSE

The onset of angina pectoris is more often sudden than gradual and is usually due to a small coronary thrombosis insufficient to cause cardiac infarction The patient may say he was capable of climbing mountains a week ago yet now he can scarcely walk 100 yards Less commonly pain is first experienced during unusually heavy exertion and gradually becomes more easily provoked This represents the slow development of occlusive atherosclerosis

The subsequent course is apt to be punctuated by short periods of relatively sudden deterioration followed by long periods of gradual improvement these episodes signify thrombotic occlusion of a medium sized coronary artery followed by the development of a collateral circulation (Schlesinger 1938) and perhaps by recanalisation

Sooner or later in the majority of cases thrombosis occludes one of the

$V_R$ I $V_L$

$V_1$ $V_2$ $V_3$ $V_4$ $V_5$ $V_6$

II $V_F$ III

(a) AT REST

$V_R$ I $V_L$

$V_1$ $V_2$ $V_3$ $V_4$ $V_5$ $V_6$

II $V_F$ III

(b) AFTER EFFORT

Fig 15 03—Electrocardiogram (a) before and (b) after exertion in a case of angina pectoris the control record (a) is practically normal the second record (b) shows significant depression of the ST segment

main coronary arteries and cardiac infarction results but a major thrombosis may occur without infarction, infarction may occur without thrombosis and ventricular fibrillation may terminate the illness in the absence of both (Appelbaum and Nicolson 1935 Nathanson 1936)

Angina may cause total incapacity in really severe cases and may finally occur at rest (status anginosus or acute coronary insufficiency)

Some cases severe or otherwise, improve after cardiac infarction others *lose their pain on developing congestive heart failure It is not clear why* this should be so but the explanation may be related to the fact that ligation of the coronary vein appears to improve the coronary circulation (Beck and Mako 1941)

## PROGNOSIS

The average life expectancy from the onset of angina pectoris is nine to ten years (White Bland and Miskall 1943) about 10 per cent live well nigh twenty years, e g John Hunter 1773–93, Sir James Mackenzie, 1907–25 Sir Thomas Lewis 1927–45 Of 6 882 cases followed for 5 to 23 years at the Mayo Clinic the mortality was 15 per cent in the first year and 9 per cent per annum thereafter (Block *et al* 1952) Women have a better prognosis than men and subjects over 40 years of age at the onset fare better than those under 40 (Parker *et al* 1946) Cardiac infarction hypertension enlargement of the heart changes of rhythm bundle branch block and other electrocardiographic abnormalities (at rest) all influence the prognosis adversely (Montgomery Dry and Gage 1947)

## TREATMENT

*Conservative* The majority of patients with uncomplicated angina of mild or moderate severity are able to carry out sedentary or light manual work Any mental or physical activity that increases the frequency of attacks or that causes pain directly should be avoided whilst adequate rest and relaxation should be assured Diet should be light and its fat content low although hypercholesterolæmia is difficult to influence by such means atherogenic macromolecular lipoproteins of the $S_f$ 10–20 class tend to be inhibited (Gofman *et al* 1950) Alcohol in moderation is not harmful in fact as a vasodilator it may be beneficial although it does not prevent electrocardiographic S T segment depression on effort (Russek *et al* 1950) Contributory factors such as hypertension obesity anæmia diabetes mellitus and anxiety should be corrected as far as possible

*Cigarette smoking* should be limited to 10 to 15 per day or given up altogether if it is found to precipitate attacks Intravenous nicotine bitartrate (2 mg) equivalent to five inhalations from a cigarette in one minute quickens the heart rate by about 15 beats per minute raises the blood pressure by an average of 12/8 mm Hg increases the cardiac output 1 to 2 litres per minute, and frequently causes dizziness or el ht

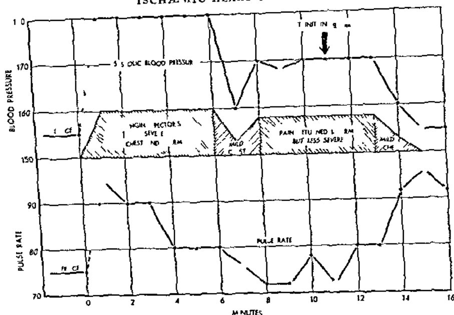



Fig 15 04—Graph showing close correlation between the height of the blood pressure and the degree or extent of pain during an attack of angina pectoris treated with trinitrin

faintness in ischæmic cases angina pectoris is provoked in 8 per cent and the electrocardiogram significantly altered in 12 per cent (Boyle *et al* 1947) Smoking cigarettes also inhibits diuresis an effect that has been attributed to stimulation of the posterior pituitary (Walker 1949) libera tion of vasopressin (pitressin) may also explain the prolonged reduction of coronary blood flow that occurs in dogs (Bulbring Burn and Walker 1949) Since ischæmic heart disease is now alleged to be at least one and a half times more common in cigarette smokers than non smokers it may be wise to abandon the habit altogether As with lung cancer cigars and pipe smoking seem relatively innocuous

*Trinitrin 1/100 to 1/120 of a grain* (0 5 mg) introduced by Murrell in 1879 may be slipped under the tongue as required either to relieve an attack or before some unavoidable effort which might induce one Trinitrin is absorbed quickly through the oral mucosa and acts as a coronary vasodilator relieving pain without necessarily altering the blood pressure (Wayne and Laplace 1933–34) but if the blood pressure is lowered as well so much the better (fig 15 04) Ischæmic S T depression in the electro cardiogram is corrected quickly (fig 15 05) Trinitrin tablets (B P) deteriorate with age losing about 10 per cent of their potency per annum preparations such as angised (B W) and nitrocine (M C) overcome this drawback

*Amyl nitrite 5 minims* (0 3 ml) is also effective but less convenient (fig 15 06) a capsule may be broken in a handkerchief and inhaled the noise of the procedure the pungent smell of the vapour and the

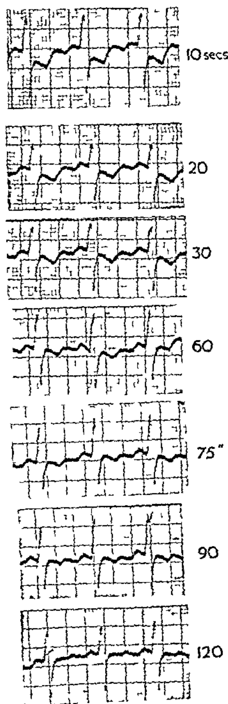



Fig 15 05—Graph illustrating rapid correction of ischæmic depression of the S T segment in lead $V_4$ in a patient with angina pectoris by means of trinitrin

vivid facial flush that accompanies its use are apt to embarrass the patient in public Amyl nitrite is a powerful vasodilator and relief of pain is associated with considerable tachycardia and conspicuous elevation of the cardiac output Much interest is also attached to the frequent paradoxical effect of amyl nitrite on the electrocardiogram for the depression of the S T segment that occurs during an attack of angina often becomes further depressed when the drug is inhaled and pain passes off (fig 15 07)

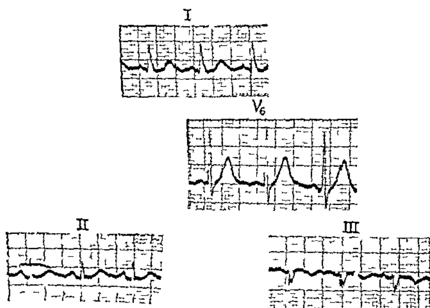
Few of the drugs used as longer acting coronary vasodilators are of much value (Master Jaffe and Dack, 1939) *Aminophylline* has the best reputation and is employed widely in doses of 0 1 to 0 2 G t d s It is difficult to demonstrate a physiological effect with such doses but severe angina may be relieved by 0 3 G four hourly if the patient can tolerate it Epigastric pain and nausea prohibit larger doses Aminophylline however may be given in conjunction with aluminium hydroxide as *theodrox*, and in this form 0 G is usually well tolerated Theophylline may also be given as *etophylate* this is the neutral salt of theophylline ethanoic acid and the base diethylene diamine and may be taken orally in doses of 0 25 to 0 5 G t d s without dyspepsia *Choline theophyllinate* in oral doses of 0 2 to 0 5 G t d s is also said to be well tolerated

$V_R$ I $V_L$

$V_1$ $V_2$ $V_3$ $V_4$ $V_5$ $V_6$

II $V_F$ III

AT REST




AFTER AMYL NITRITE

Fig 15 06—Electrocardiogram during an attack of myocardial ischæmia treated with amyl nitrite
Expected response showing prompt correction of the depressed S T segment

Amongst the long acting nitrites and nitrates there is *pentaerythritol tetranitrate* (nitropent) which has a mild coronary vasodilator action lasting for about four hours In Great Britain it is marketed as mycardol (Bayer) and peritrate (Warner) the former is made up in 30 mg tablets the latter in 10 mg tablets In oral doses of 10 to 30 mg one hour before meals nitropent not only tends to relieve pain but also inhibits electrocardiographic S T segment depression on exercise (Russek *et al* 1955) Larger doses of nitropent usually cause dyspepsia

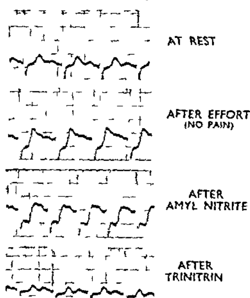



Fig 15 07—Paradoxical effect of amyl nitrite on depression of the S T segment in a case of angina pectoris

Recent reports have claimed that khellin an extract from the seeds of an Eastern Mediterranean wild plant *ammi visnaga* is an effective coronary vasodilator with a prolonged action The dose is 100 mg by mouth three times daily Angina pectoris is said to be relieved in 74 per cent of cases (Anrep *et al* 1946 1947) Unfortunately khellin is so badly tolerated by the majority of patients that in its present form it can hardly be considered a therapeutic agent

Enthusiastic reports from Canada concerning the beneficial effect of vitamin E in doses of 200 to 600 mg (Shute 1945) have not been confirmed

Since *œstrogens* not only inhibit experimental atherogenesis in cockerels but also reduce the severity of atherosclerotic lesions already present (Katz and Stamler 1953) they have naturally been tried therapeutically in man and as previously stated they tend to restore the normal blood lipid pattern (Barr 1953) Improvement of ischæmic heart disease however has not yet been demonstrated and the side effects such as mammary development in the male are undesirable There may be a stronger case for the use of œstrogens in cases of angina pectoris in relatively young women who have undeveloped ovaries or who have had bilateral oophorectomy

*Testosterone propionate* has no place in the treatment of angina pectoris for androgens are contra indicated

Other agents that may inhibit atherogenesis or actually help to clear lesions already present are under trial they include inositol (Felch *et al* 1952) beta sitosterol (Barber and Grant 1955) and heparin (Engelberg 1952) No such drug can yet be recommended therapeutically

*Artificial myxœdema* Total ablation of the thyroid gland was introduced

by Blumgart Levine and Berlin (1933) in the hope that an appreciable reduction on the circulatory demands would benefit cases of angina pectoris (and congestive heart failure) Fair results were obtained (Cutler and Schnitker 1934) improvement being partly attributed to decreased sensitivity to adrenaline (Eppinger and Levine 1934) The operation gained little favour in England The high blood cholesterol that results does not favour the natural course of the disease and the doubtful benefits obtained hardly justify the risks and complications of total thyroidectomy

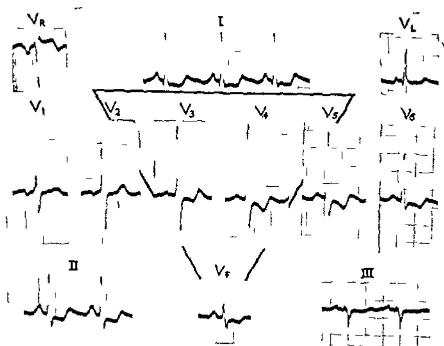



Fig 15 08—Acute coronary insufficiency showing persistent inversion of the S T segment in all indirect surface leads

Thiouracil however offers a simple and more easily controlled means of achieving the same object and can be abandoned at any time if the result is unsatisfactory (Raab 1945 Ben Asher 1947) The dose recommended is 200 to 600 mg of methyl or propyl thiouracil daily beginning with the larger dose and gradually reducing it to the minimum that proves effective If more heroic doses are required equal quantities of propyl and methyl thiouracil may be given together in the hope of avoiding toxic reactions such as fever rash and agranulocytosis the principle being that drug combinations (e g sulphonamide mixtures) cause less sensitisation than the same total dose of a single member of the group while retaining the same therapeutic effect (Lehr 1948) Cases of severe angina pectoris do not tolerate thiouracil fever well In the experience of the author fever and

rash are less common with propyl than with methyl thiouracil Mercazole 20–30 mg three times daily, finally reduced to about 10 mg t d s is equally effective and seems relatively free from complications

The blood cholesterol should be watched and if it rises above 300 mg per cent the question of reducing the dose of thiouracil or mercazole should be considered A low fat diet may help to keep the blood lipids within bounds

Radioactive iodine ($I^{131}$) performs the same service as thyroidectomy and is equally permanent It may be given in a single dose of 20 millicuries or in three divided doses of 10 millicuries at weekly intervals The B M R may then be maintained at minus 20–25 per cent by means of small doses of thyroid In view of the poor prognosis in these difficult cases the danger of late malignancy may be disregarded In their latest review of 7 0 resistant cases of angina pectoris treated by means of artificial myxœdema Blumgart *et al* (1955) reported a good result in 75 per cent I have never myself been able to develop much enthusiasm for this form of treatment partly because of the rise in blood cholesterol that usually takes place and partly because it is very difficult to keep patients relatively free from pain without provoking distressing features of myxœdema but then I have o ly embarked on antithyroid treatment in advanced cases that have been almost totally incapacitated

*Surgical methods* Several surgical procedures designed to relieve angina have been evolved in recent years Few have gained much support but there is something to be said in favour of abolishing pain by sensory denervation of the heart achieved by means of section of the upper four dorsal spinal nerve roots or by stellate and upper dorsal ganglionectomy (White Garrey and Atkins 1933) Destruction of the ganglia by alcoholic injection is less certain and may cause intractable root pain in about 10 per cent of cases Despite the theoretical argument that ganglionectomy may remove nature s warning signal and so allow patients to exercise themselves beyond the limits of safety there is no doubt that some cases do remarkably well (White and Bland 1948 Lindgren 1950) Sensory denervation of the heart does not entirely abolish the subjective recognition of an anginal attack although the sensation experienced is not painful There is good reason to believe also that sympathectomy tends to prevent ventricular fibrillation (Leriche *et al* 1931, McEachern 1940), and seems to improve the coronary circulation either by preventing reflex spasm (Levy and Moore 1941) or by causing coronary vasodilatation (Katz and Jochim, 1939)

A more drastic surgical procedure aims at improving the coronary circulation by supplying it with a new source of collateral vessels The idea was based on necropsy observations which showed that the heart might function remarkably well despite almost complete coronary occlusion if for some reason an adequate collateral circulation had developed through the pericardium These natural results of accident and disease have been mar

shalled and developed by Claud Beck (1935–36) in the U S A and by O Shaugnessy (1936–37) in England Beck sutured a flap of pectoral muscle to the surface of the heart O Shaugnessy preferred cardio omentopexy the omentum being brought up through the diaphragm and stitched or glued on to the surface of the heart after scarification Whilst experimental evidence affords convincing proof of the establishment of a collateral circulation by such means the results obtained in clinical cases of ischæmic heart disease scarcely justify the risk entailed

A simpler means of achieving the same object is to introduce bone dust into the pericardial sac when the pericardial reaction subsides vascular adhesions offer a collateral source of blood supply to the myocardium (King 1941) Powdered magnesium silicate serves equally well (Thompson and Plachta 1953)

## ACUTE CORONARY INSUFFICIENCY

The term *acute coronary insufficiency* (Master *et al* 1947) is now widely used to describe those cases of ischæmic heart disease that cannot properly be called angina pectoris or cardiac infarction but rather something between the two Some cases are subacute or even chronic

*Physiologically* the coronary circulation is insufficient to meet the full demands of the myocardium at rest, yet sufficient to prevent myocardial necrosis Since the situation commonly develops relatively suddenly it is usually attributed to coronary thrombosis or possibly to subintimal hæmorrhage

Special forms of acute coronary insufficiency may be caused by any agent that temporarily interferes with the coronary blood flow e g hæmorrhage (Master *et al* 1950) shock (Wiggers 1947) vaso vagal syncope asphyxia and carbon monoxide poisoning especially if the work of the heart is increased simultaneously as in paroxysmal tachycardia atrial flutter (or fibrillation) massive pulmonary embolism and ruptured aortic cusp greatly increased cardiac work alone may also cause coronary insufficiency (especially when there is latent coronary disease) as in hypertensive or thyrotoxic crises

*Clinically* the onset is usually acute or subacute from a state of normal or relatively good health the patient suddenly finds himself unable to walk more than a few yards without pain and may have prolonged attacks of angina at rest particularly after food and when he lies flat, but the pain is still relieved by trinitrin There is no fever leucocytosis elevation of the sedimentation rate or increased transaminase activity the blood pressure does not fall there is no pericardial friction or other clinical evidence of cardiac infarction and the electrocardiogram shows nothing more than ischæmic depression of the RS T segment in left ventricular surface leads or their equivalents (fig 15 08) These electrocardiographic changes usually persist for several days or weeks and are not confined to attacks of pain

VR I VL

V1 V2 V3 V4 V5 V6

II VF III

Fig 15 9—Transient inversion of the T waves in all chest leads in a case of acute coronary insufficiency

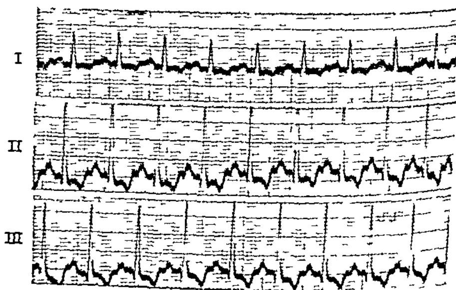



Fig 15 10—Electrocardiogram showing transient inversion of the T waves following prolonged circulatory collapse with extreme tachycardia without evidence of structural disease of the heart

Transient inversion of the T waves proper, without abnormal Q waves and without elevation of the RS T segment may also occur in coronary insufficiency (fig 15 09) but is more difficult to interpret for it is also compatible with a small cardiac infarction Simple transient inversion of the T waves is common in the special forms of coronary insufficiency mentioned above (fig 15 10) especially following prolonged paroxysmal tachycardia in paroxysmal hypertension from pheochromocytoma and in carbon monoxide poisoning (fig 15 11)

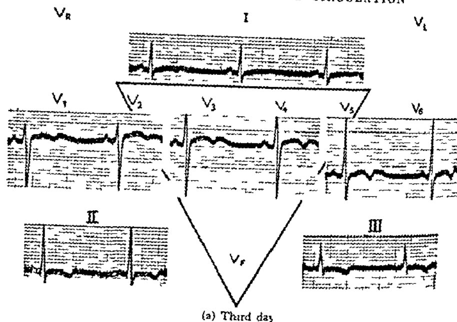
*Treatment*

Patients with acute coronary insufficiency should be put to bed for a minimum period of three weeks and treated with anticoagulants (page 746) in order to prevent extension of thrombosis the fear that a subintimal hæmorrhage may be aggravated by such treatment is not substantiated in practice Treatment should be continued for at least three weeks after attacks of pain have ceased which may mean for two to three months in obstinate cases These prolonged subacute cases may be very trying to all concerned and it might seem better to abandon treatment in the hope that the ischæmic zone would then necrose and the pain cease While it is agreed that this may happen and the patient be the better for it it is unfortunately impossible to predict the consequences which are just as likely to be disastrous Controlled cardiac infarction is beyond our present therapeutic powers It is far better therefore to continue anti coagulant treatment with or without the temporary help of an antithyroid drug, for sooner or later the situation is likely to ease as the result of an improved collateral circulation

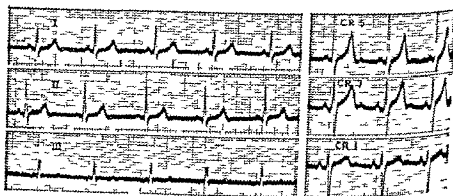
That anticoagulant therapy alters favourably the immediate outcome and future course of cases of acute coronary insufficiency has not yet been proved but I have little doubt that it does Cardiac infarction is preceded by symptoms of acute coronary insufficiency in at least one quarter of all cases (Mounsey 1951) of a personal series of 25 cases of acute coronary insufficiency not treated with anticoagulants no less than 12 developed acute cardiac infarction within three weeks and five of these died of 33 similar cases treated with anticoagulants only two developed cardiac infarction within the month neither of which died and a third steadily deteriorated and died suddenly a week after the onset of treatment Both series are small because the criteria on which the diagnosis was based were strict (Wood 1948)

*Prognosis*

Long term follow up studies of cases proved at the time to have acute coronary insufficiency rather than cardiac infarction await analysis The immediate outcome depends largely on whether cardiac infarction develops or not as explained above Less than 5 per cent die abruptly from ven tricular fibrillation without infarction




(a) Third day




(b) Twelve days later

Fig 1 11—Transient inversion of the T waves due to carbon monoxide poisoning

## CARDIAC INFARCTION

Myocardial infarction occurs when a mass of heart muscle is sufficiently deprived of its blood supply for an adequate time The common cause of such an event is coronary thrombosis but coronary embolism subintimal hæmorrhage in an atherosclerotic vessel dissection and critical lowering of the blood-pressure as from shock or hæmorrhage in a patient with occlusive coronary atherosclerosis or syphilitic aortitis may each produce it Again coronary thrombosis does not cause myocardial infarction if the collateral circulation is sufficient to preserve the life of the threatened tissue It follows that coronary thrombosis and myocardial infarction are

not synonymous terms and should not be confused the former means no more than its literal sense implies the latter means death of a localised mass of heart muscle

## ANATOMY OF THE CORONARY CIRCULATION

The site and extent of the infarct depend upon the vessel or vessels occluded upon the capacity and efficiency of collateral channels and upon the anatomy of the coronary circulation

There are two main coronary arteries left and right The left divides early into an anterior descending branch and into a left circumflex the large anterior descending branch runs down the interventricular groove to the apex of the heart and nourishes the anterior part of the right ventricle the interventricular septum and the anterior and apical part of the left ventricle the smaller left circumflex branch curls round the back between the left atrium and ventricle and supplies the upper lateral and posterior basal portion of the left ventricle The right coronary artery does not divide but runs round to the back between the right atrium and ventricle sending branches to the region of the sinus node to the anterior part of the right ventricle and to the posterior base of both ventricles There is a considerable degree of anastomosis between the terminal branches of these vessels an anastomosis that increases rapidly when the blood supply to any area is threatened (Prinzmetal *et al* 1947) The right ventricle supplied as it is by the two biggest coronary arteries and offering little resistance to systolic coronary blood flow is rarely the seat of infarction The upper and lateral part of the left ventricle is supplied by proximal branches from both anterior descending and left circumflex vessels and is therefore relatively safe The posterior basal region is less secure for it is supplied only by terminal branches, some from the right coronary artery and some from the left circumflex In having this double source of nourishment however it is still more fortunate than the anterior apex of the left ventricle which is fed almost entirely by terminal rami from the anterior descending branch of the left coronary artery although anastomotic channels can develop rapidly from the posterior descending branch of the right coronary artery The interventricular septum is supplied anteriorly by perforating branches from the anterior descending coronary artery and posteriorly by perforating branches from the right Anastomoses are more conspicuous in the superficial layers of the myocardium than in the inner layers (Prinzmetal *et al* 1948) they are also at a physiological disadvantage when near the endocardium because they are subjected to a higher intramyocardial pressure (Johnson *et al* 1939)

## SITE OF THROMBOSIS AND INFARCTION

Clinically major coronary thrombosis involves the anterior descending branch of the left coronary artery in 66 to 75 per cent of cases the right coronary artery in 25 to 40 per cent and the left circumflex in 5 to 33 per cent (Barnes and Ball 1932 Appelbaum and Nicolson 1935 Munck,

1946) thrombosis of the left main trunk is relatively rare These figures a conservative for careful study of the whole coronary tree by means o radio opaque injections reveals multiple thromboses in the majority o instances

The relative incidence of the various sites of infarction harmonises with the anatomical and physiological data and with the sites of thrombosis In an analysis of 160 cases Wartman and Hellerstein (1948) found chiefly anterior infarction in 72 per cent and chiefly posterior infarction in 8 per cent but there were multiple infarcts in 41 per cent Half the anterior infarcts and a quarter of the posterior infarcts also involved the inter ventricular septum Right ventricular infarction rarely occurs alone b t may complicate anteroseptal infarction of the left ventricle (Zaus and Kearns 1952) Atrial infarction has also been described (Hellerstein 1948)

Combining figures published by Appelbaum and Nicolson (1935) Nathanson (1936) Clawson (1939) and Munck (1946) it is found that coronary thrombosis occurs without cardiac infarction in 20 per cent of cases and that cardiac infarction occurs without coronary thrombosis in 29 per cent in the latter group atherosclerotic occlusion may be comple or incomplete

## *PATHOLOGY*

A cardiac infarct may be difficult to distinguish with the naked eye when less than twenty four hours old microscopically however acute necrosis of the muscle fibres may be recognised by their swollen appearance and by the loss of their nuclei and striations When a few days old an infarct is discoloured and may be surrounded by a red zone of hæmorrhage or congestion Microscopically the necrosed muscle is seen to be invaded by polymorphs Older infarcts are yellowish white in colour and represent scar tissue

When necrosis involves the inner layers of the myocardium mural thrombi frequently form against the damaged endocardium in fact they are found in 40 to 50 per cent of all cases (Hellerstein and Martin 1947) Local pericarditis occurs over superficial necrosis and has been reported in 30 to 75 per cent of all cases (Wartman and Hellerstein 1948 Stewart and Turner 1938) diffuse pericarditis develops in about 10 per cent

Myocardial softening (myomalacia cordis) may result in rupture of the heart (5 to 15 per cent) or in the formation of a cardiac aneurysm (10 to 30 per cent according to published necropsy figures and according to the definition of an aneurysm)

*Precipitating agents* If due allowance is made for the average time occupied by sleep ordinary activities and physical effort during each twenty four hours then coronary thrombosis (at least in men under 4 ) occurs six times more frequently during physical effort than during sleep and twice as frequently during physical effort as during ordinary day to-day

activities (Yater *et al* 1948) Unaccustomed effort particularly, may precipitate an attack

The peak incidence of coronary thrombosis is in December (Brown and Pearson 1948) but according to Teng and Heyer (1955) is more related to sudden changes of temperature than to the cold *per se* Certainly going out into the cold after leaving a warm room very commonly provokes an attack of angina pectoris in ischæmic subjects Clearing the drive of snow includes both unaccustomed effort and the change from a warm to a cold temperature and is a known precipitating cause of coronary thrombosis

A heavy meal is often blamed but statistical evidence on the point is not available Sexual intercourse is in the same category Both are notorious causes of an attack of angina pectoris There is likewise as yet no proof that a prolonged period of excessive mental stress can be responsible although experience favours the view that it can

Other known precipitating agents include surgical shock the post operative state trauma and a sudden fall of blood pressure

*SYMPTOMS*

Although the onset of cardiac infarction is sudden premonitory symptoms are common during the preceding week or so and take the form of typical or atypical angina pectoris Then or without warning of any kind and often without any obvious precipitating cause the major attack overwhelms the patient and is commonly signalled by pain indistinguishable in site radiation and quality from angina pectoris but instead of passing off in a few minutes it lasts for hours Its intensity varies from a feeling of pressure to extreme agony and gives no indication of the size of the infarct There may be no other symptoms on the other hand there may be collapse weakness faintness sweating restlessness breathlessness and vomiting Whilst a classical attack is characterised by pain others present with syncope and yet others with suffocation In the syncopal type which represents a vaso vagal reaction loss of consciousness may prevent appreciation of pain when paroxysmal cardiac dyspnœa or acute pulmonary œdema dominates the scene the patient usually admits pain on close questioning The lack of agreement in the literature concerning the frequency of painless infarction (0–61 per cent) may be explained by the heterogeneous manner in which historical data is collected and by lack of uniformity with regard to the definition of the word *painless* In about one third of all cases patients deny pain in its ordinary sense preferring words like discomfort pressure tightness oppression or heaviness—as in angina pectoris Less than 5 per cent of cases of cardiac infarction have no ischæmic sensation at all about half of these are entirely silent and discovered by routine electrocardiography

*PHYSICAL SIGNS*

Unlike angina pectoris myocardial infarction provides a wealth of physical signs and special findings When first seen the patient is usually

grey cold sweating obviously ill and in pain he may be breathless and cyanosed or he may be pale and collapsed—perhaps unconscious on the other hand he may present none of these features Within two or three days mild cases may look and feel well

The jugular venous pressure is sometimes a little raised during the first day or two and the pulse rate accelerated but in cases with a vaso vagal reaction there may be bradycardia There may be orthopnœa paroxysmal cardiac dyspnœa or frank pulmonary œdema in severe cases

The *blood pressure* falls initially only in cases with a vaso vagal reaction and indeed may be elevated during the first twelve hours or so (Weiss 1939) in animals it is similarly maintained for the first twenty four hours (Gross *et al* 1938) but it drops later commonly reaching its lowest level on the third or fourth day, when systolic pressures of 80 to 90 mm of mercury are often found Thereafter it remains low for several days or even for weeks and then in all who survive climbs slowly back towards its previous level which it may or may not reach (fig 15 12) In 67 per cent of fatal cases Chambers (1947) observed no such recovery In hypertensive subjects this drop in pressure may not be recognised unless the original level is known

The *heart sounds* are often faint particularly when the blood pressure is low and there may be presystolic or diastolic gallop rhythm Transient *pericardial friction is heard in about 10 per cent of cases* especially when the infarct is anterior *Disturbances of rhythm* are not uncommon and include ectopic beats paroxysmal ventricular tachycardia auricular flutter or fibrillation and any grade of heart block

*Low grade fever* is the rule and may continue for several days but rarely for more than a week Transient polymorphonuclear *leucocytosis* also occurs during the first few days and the C-reactive protein test is positive The *sedimentation rate* begins to accelerate after a day or two reaches maximum velocity towards the end of the first week and then gradually returns to normal in an average period of six weeks from the onset (fig 15 13) (Wood 1936)

During the first 48 hours the *serum glutamic oxalacetic transaminase* (S G O T) *activity is sharply increased from the normal of 10 to 40 units* to any level up to 800 units the height to which it rises being *proportional to the mass of necrosed myocardium* (La Due *et al* 1954 1955) S G O T is an enzyme employed in the synthesis of glutamic and oxalacetic acid and is widely distributed in the tissues especially in heart muscle It is not increased in infectious neoplastic metabolic or degenerative diseases unless there is destruction of cardiac hepatic or muscular tissue

## *ELECTROCARDIOGRAPHIC APPEARANCES*

These have already been described and explained in Chapter III Leads facing the surface of the infarct show a prominent or monophasic Q wave initial elevation of the RS T segment and subsequent inversion of the T

wave Anterior infarcts may be mapped out with precision by means of multiple unipolar chest leads and may be chiefly anterolateral (fig 15 14) or anteroseptal (fig 15 15) The Q T pattern is usually transmitted to lead $V_L$ and hence mainly to standard lead I But if the heart is electrically vertical a $V_5$ Q T pattern may be transmitted to lead $V_F$ and hence to standard leads II and III The Q T pattern of posterior infarcts is seen in œsophageal leads over the posterior surface of the left ventricle and is transmitted to lead $V_F$ and hence to standard lead III (fig 15 16) while chest leads usually show initial depression of the RS T segment followed by unusually tall T waves (fig 15 17)

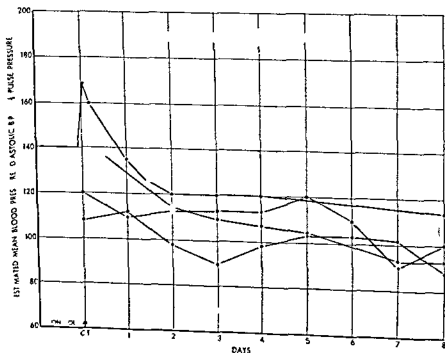



Fig 15 12—Behaviour of the blood pressure in four cases of acute myocardial infarction

The abnormal Q wave develops early and may persist indefinitely Elevation of the R T segment is usually transient but a monophasic Q wave associated with persistent elevation of the Q T segment is often seen with ventricular aneurysm (fig 15 18) Primary inversion of the T wave appears in a few days reaches a maximum within two or three weeks and then gradually reverts towards normal but slight inversion with Pardee coving of the RS T segment may persist in one or more leads (fig 15 19)

The diagnosis of acute cardiac infarction is practically untenable if serial electrocardiograms remain normal in all the recognised leads but an initial electrocardiogram may be normal occasionally if taken within a few hours

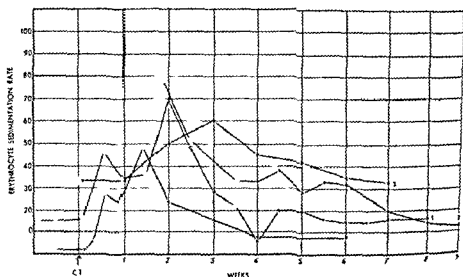



Fig 15 13—Behaviour of the sedimentation rate in four cases of acute myocardial infarction

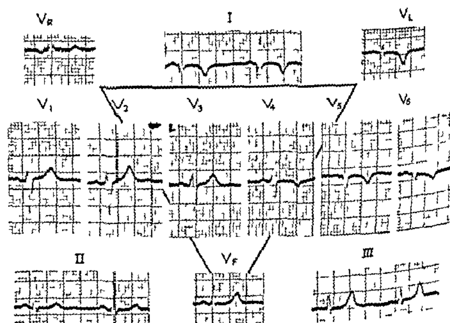



Fig 15 14—Electrocardiogram showing anterolateral cardiac *infarction* Maximum changes are seen in leads $V_3$ $V_4$ $V_L$ and standard lead I

of the onset This statement may have to be tempered in the light of Prinzmetal's evidence that the inner third of the myocardium may be electrically silent (Prinzmetal *et al* 1953) at least in respect of the initial

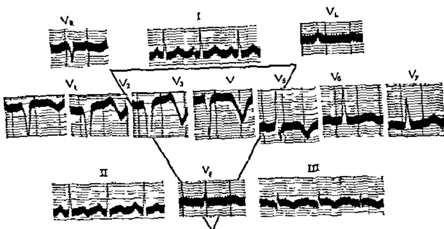



Fig 15 15—Electrocardiogram showing anteroseptal cardiac infarction Maximum changes are seen in leads $V_3$ and $V_4$

ventricular complex The belief that subendocardial infarcts cause depression of the RS T segment in overlying surface leads (Levine and Ford 1950) is not supported by Prinzmetal's experimental work (Rakita *et al* 1954)

In differential diagnosis great stress is laid on the abnormal Q wave for this always means appreciable necrosis of heart muscle however produced It must of course be distinguished from a normal Q wave measuring 2 or 3 mm and a monophasic downward deflection in standard lead III should not be accepted as a Q wave unless Q is also prominent in standard lead II and in lead $V_F$ (fig 15 20) Pathological Q waves however *may* be seen occasionally in cases of myocardial necrosis caused by non ischæmic agents e g isolated myocarditis amyloidosis, tumour, hydatid, and other rare cardiopathies*

Elevation of the RS T segment is also seen in pericarditis and opposite large S waves in appropriate leads in left ventricular preponderance and left bundle branch block but the contour of the S T segment and the general pattern is different as described elsewhere

Primary inversion of the T wave alone is less conclusive evidence of infarction for it may be seen in a variety of conditions including toxic myocarditis pericarditis, carbon monoxide poisoning myxœdema, certain biochemical states most of the relatively obscure cardiopathies, and following paroxysmal tachycardia. However the depth and sharpness of the inversion usually exceed that in all other types and its association with upward coving of the RS T segment is practically diagnostic Changes in

Fig 15 16—Electrocardiogram showing posterior cardiac infarction Characteristic changes are seen in leads $V_F$ and hence in leads II and III The ST segment is depressed in lead $V_4$

serial graphs are less helpful because many of the primary T wave changes mentioned above are also transient*

*Bundle branch block* mostly left occurred in 7 3 per cent of 700 cases of angina pectoris and in 8 9 per cent of 528 cases of cardiac infarction reported by Salcedo Salgar and White (1935) Conversely they found that ischaemic heart disease accounted for approximately 50 per cent of 181 cases of intra ventricular block of all types Master, Dack and Jaffe (1938) found the

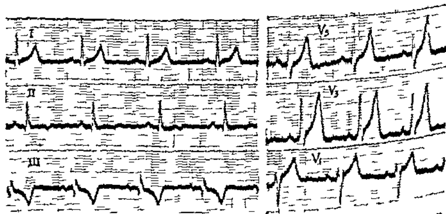
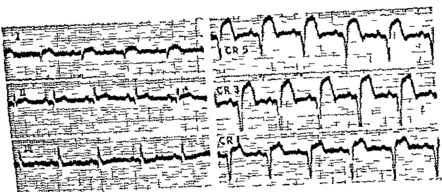
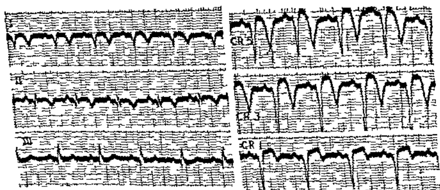


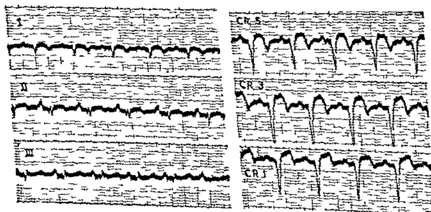

Fig 15 17—The later stage of posterior infarction showing unusually tall T waves in chest leads




(a) 29th November 1941




(b) 15th December 1941




(c) 3rd March 1942

Fig 15 18 Electrocardiogram showing widespread monophasic Q waves and persistent levation of the ST segment associated with ventricular aneurysm

VR I VL

V1 V2 V3 V4 V5 V6

II VF III

Fig 15 19—Electrocardiogram of a case of old cardiac infarction showing persistent Q waves and Pardee coving of the ST segment in anterior left ventricular surface leads and their counterparts (leads $V_L$ and standard lead I) The infarct occurred 14 months previously

VR I VL

V1 V2 V3 V4 V5 V6

II VF III

Fig 15 20—Electrocardiogram in a case of pregnancy showing a prominent Q wave and inversion of the T wave in lead 3 due to cardiac rotation note the absence of a pathological Q wave in lead $V_F$ and the presence of an S wave in standard lead I

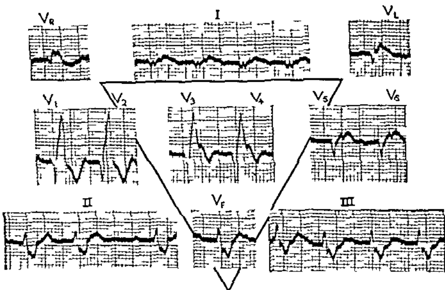



Fig 15 21—Electrocardiogram showing typical appearances of anterior cardiac infarction in the presence of right bundle branch block

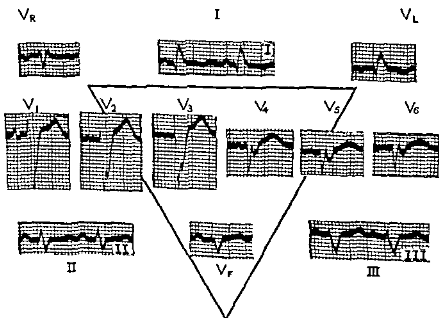



Fig 15 22—Electrocardiogram showing typical appearances of anterior cardiac infarction in the presence of left bundle branch block

incidence of bundle branch block in acute coronary occlusion to be 1 per cent in 1,058 cases collected from the literature, and 15 per cent in 313 cases of their own Intraventricular block does not necessarily imply septal infarction in these cases and of course may precede the acute episode Its importance lies in the fact that it may mask the electrocardiographic signs of cardiac infarction for as explained on page 99 there can be no Q wave in leads facing the surface of the left ventricle in cases of left bundle branch block unless the septum is also necrosed and the gross deformity of the R T component may overshadow RS T changes due to the infarct Somerville and Wood (1949), however found that the characteristic Q T pattern of an infarct could be recognised in nearly all cases complicated by right bundle branch block (fig 15 21) and in about half those with left bundle branch block (fig 15 22)

Electrocardiography may be of great value in the diagnosis of myocardial infarction months or years after the event an abnormal Q wave, local dwarfing of R or primary inversion of the T wave in one or more left ventricular surface leads or their counterparts being particularly helpful Complete restitution of the normal electrocardiographic pattern occurs in only 10 per cent of survivors from acute myocardial infarction (Mills *et al* 1949)

## *RADIOLOGICAL FINDINGS*

Fluoroscopy is impracticable during the acute stage of the illness but may be useful later An infarct on the left border of the heart near the apex may form a ledge (fig 15 23) In normal hearts pulsation is seen around the whole surface of the left ventricle in myocardial infarction there may be local absence of pulsation or pulsation may be locally paradoxical a portion of the ventricle expanding while the rest contracts this area of absent or paradoxical pulsation represents the infarct and may be seen on the left border of the heart towards the apex or on the diaphragmatic surface of the left ventricle (with the aid of gas in the stomach) for some reason posterior basal infarcts are less easily visualised Interpretation of pulsation as seen on the fluoroscope is by no means easy and requires considerable experience of normal variation The kymograph a simple device for obtaining a permanent skiagraphic record of cardiac pulsation has been used with some success as an aid in analysing the findings and the electrokymograph is even better but absence of pulsation at the apex may also be seen occasionally in hypertensive and other forms of heart failure

Ventricular aneurysm is more easily recognised particularly when situated towards the apex or left lateral border (fig 4 34) It should not be confused with a dilated left atrium an intrapericardial hæmatoma pericardial cyst or cardiac tumour Rarely a ventricular aneurysm may become calcified (fig 4 35) Increased density and unfolding of the aorta due

to atheroma with or without calcification may be seen in many cases, but cannot be regarded as evidence of coronary atherosclerosis calcified coronary arteries (Snellen and Nauta 1937) offer more convincing proof but even these do not necessarily signify ischæmic heart disease

Apart from the changes mentioned the size and shape of the heart are usually normal in cases of uncomplicated cardiac infarction (Miller and Weiss 1928) enlargement is commonly due to heart failure or to coincident hypertensive heart disease

With the aid of retrograde aortography via the right radial artery the entire coronary tree may be seen and the exact site of any obstruction identified (Coelho *et al*, 1953) but the method is certainly not without risk and cannot be recommended as a safe diagnostic procedure

## COMPLICATIONS

*(first 28 days)*

| | PERIOD (early mid or late) | FREQUENCY (per cent) | MORTALITY (per cent of all cases) |
|---|---|---|---|
| *Abrupt death* (ventricular fibrillation or asystole) | Onset<br>Early or mid | ?25<br>10 | ?25<br>10 |
| *Shock* | Early | 10 to 15 | 7 to 12 |
| *Conventional heart failure* | Mid and late | 10 to 15 | 3 to 5 |
| *Rupture* | | | |
| of heart | Early | 1 5 to 3 | 1 5 to 3 |
| of septum | Early | Rare | Rare |
| of papillary muscle | Early | Rare | *Rare* |
| *Cardiac aneurysm* | Early (recognised late) | 5 to 10 | (See rupture those recognised commonly survive) |
| *Pericarditis* | Early | 10 | (See rupture majority survive) |
| *Thrombo-embolism* | | | |
| Pulmonary | Mid and late | 15 | 2 to 3 |
| Systemic (chiefly cerebral) | Mid | 5 to 10 | 1 to 2 |
| *Changes of rhythm* | | | Changes of rhythm increase the mortality from cardiogenic shock and heart failure |
| Atrial fibrillation | Early | 10 | |
| Atrial flutter or tachycardia | Early | 2 | |
| Ventricular tachycardia | *Early* | 2 | |
| Complete heart block | Early | 1 | |
| TOTAL (excluding abrupt death at onset) | — | — | 25 to 30 |

## *COURSE AND COMPLICATIONS*

The acute stage lasts on the average for six weeks during the earlier part of which many complications may arise (see table) the gravest danger being abrupt death from *ventricular fibrillation* (fig 15 24) About 10 per cent of all cases that survive long enough to be admitted to hospital die in this way and there must be many others that go to the coroner Thus of 866 cases in relatively young men reported by Yater *et al* (1948) 16 per cent *died at once and another 10 per cent within 15 minutes none of these* cases would have had time to be admitted to hospital If coroners cases are included therefore it is likely that at least one third of all cases of acute cardiac infarction die from ventricular fibrillation or asystole

*Other disturbances of rhythm* are also relatively common and include ventricular ectopic beats paroxysmal ventricular tachycardia (2 per cent), paroxysmal auricular flutter (2 per cent) and fibrillation (10 per cent) nodal rhythm and heart block They should be regarded seriously because *they may herald ventricular fibrillation or precipitate heart failure* Complete heart block (1 per cent) is particularly lethal (Mintz and Katz 1947)

*Shock* attending the first stage of acute cardiac infarction is characterized clinically by pallor sweating vomiting coldness of the extremities and exposed surfaces faintness or loss of consciousness great weakness restlessness oliguria or anuria small pulse tachycardia or bradycardia and low blood pressure physiologically the cardiac output is much reduced the peripheral resistance raised the circulation time prolonged and the venous pressure raised (Freis *et al* 1952 Gilbert *et al* 1954) Fundamentally therefore there is a state of acute and severe heart failure although peripheral circulatory failure may complicate the picture and sweating *vomiting and a slow pulse rate suggest powerful vagal action* Cardiogenic shock occurs in 10 to 15 per cent of cases and is fatal in two thirds to three quarters of them (Selzer 1952)

*Heart failure* may present more conventionally *either* as left ventricular failure or congestive heart failure Acute left ventricular failure with pulmonary œdema may occur at the onset or a more insidious form with dyspnœa and orthopnœa may develop later not *infrequently* during convalescence Congestive failure with a rise of venous pressure distension of the liver and œdema may also be a relatively late complication and increases the risk of phlebothrombosis and pulmonary embolism Conventional heart failure distinct from cardiogenic shock, usually responds to treatment in the first instance but is a common cause of death during the ensuing twelve months During the acute stage of cardiac infarction (first 28 days) it occurs as frequently as shock (10 to 15 per cent of cases) *and proves fatal in approximately 3 to 5 per cent* It is very difficult to obtain precise figures from the literature for cardiogenic shock and conventional heart failure are frequently grouped together

*Thrombo embolic lesions* in various situations are detected clinically in about 20 per cent of cases and may be found at necropsy in about 45 per




Fig 15 23—Skiagram in a case of anterior cardiac infarction showing a ledge on the left border of the heart

cent (Hellerstein and Martin 1947) The dangerous period is from the fifth or sixth day to the end of the third week, when the clotting time is shortened (Ogura *et al* 1946) Phlebothrombosis in the legs resulting in pulmonary embolism is by far the most common clinical manifestation and is responsible for death in 2 to 3 per cent of all cases of acute cardiac infarction In a series of 200 fatal cases of coronary thrombosis reported by Eppinger and Kennedy (1938) pulmonary embolism was directly responsible for death in 6 5 per cent was present in 24 5 per cent and complicated 32 7 per cent of those with heart failure The usual frequency of pulmonary embolism in all cases of cardiac infarction that survive long enough to be admitted to hospital is 15 per cent (Evans 1954)

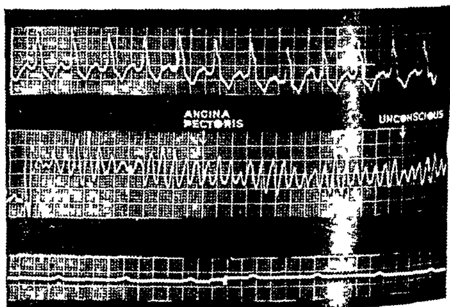



Fig 15 24—Electrocardiogram showing the mode of death in a case of ischæmic heart disease entricular fibrillation developed while a routine graph was being taken

*Systemic embolism* (or thrombosis) is detected *clinically* in 5 to 10 per cent of cases the majority of them cerebral Only 1 to 2 per cent of all cases of acute cardiac infarction die from cerebral or other systemic embolism Hellerstein and Martin give the actual incidence of various thrombo-embolic lesions as follows

| | *Per cent* |
|---|---|
| Pulmonary | 23 5 |
| Renal | 14 4 |
| Splenic | 8 8 |
| Cerebral | 7 7 |
| Peripheral arteries | 5 5 |
| Mesenteric | 1 9 |
| Carotid or aortic | 0 5 |

Mural thrombosis is found at necropsy in 44 per cent of all fatal cases of cardiac infarction and is presumed to be the source of the peripheral vascular lesions the fact that these lesions have been found in 46 per cent of cases with mural thrombosis (Wang Bland and White 1948) and in 39 per cent of cases without mural thrombosis does not invalidate this view for fresh intraventricular clots may be dislodged and leave no evidence of their origin On the other hand pulmonary embolism is nearly always attributable to phlebothrombosis in the legs not to right ventricular mural thrombosis and cerebral vascular lesions may certainly result from coincidental local thrombosis (Bean 1938)

*Cardiac rupture* occurs in 1 5 to 3 per cent or in 5 to 10 per cent of fatal cases (Oblath Levinson and Griffith 1952) usually within the first four days of the illness and chiefly in the older patients (Gans 1951) it is not necessarily a dramatic event for the perforation may be small and the signs and symptoms often those of cardiac compression from hæmopericardium rather than sudden catastrophe such cases sometimes living a week or more *Perforation of the interventricular septum* is seen occasionally and gives rise to the sudden development of a coarse systolic thrill and murmur in the third and fourth intercostal spaces towards the sternum (Fowler and Failey 1948) Heart failure has ensued rapidly in most of the cases reported (e g Leonard and Daniels 1938) Although the perforation may look small at necropsy and the track tortuous the shunt during life may be considerable as has been proved (inadvisedly) by means of cardiac catheterisation More than half the cases have died within the month

*Rupture of one of the papillary muscles* is a rare complication of cardiac infarction and results in the sudden development of severe mitral incompetence with secondary acute and intractable left ventricular failure usually ending in death (Craddock and Mahe 1953)

*Left ventricular aneurysm* may be found at necropsy in as many as 22 per cent of fatal cases (Wartman and Hellerstein 1948) but is recognised clinically in less than half of them In the series referred to above 25 were anterior and 10 posterior five of them ruptured The condition arises early and may be well developed by the time the patient is allowed up for fluoroscopy The X ray appearances have already been described (page 738) Clinically it is suggested by an unusual pulsation in the region of the apex beat when left ventricular enlargement is improbable on other grounds Scherf and Brooks (1949) described an odd high pitched gushing soft diastolic murmur over the aneurysm in three of their cases but this is unusual The electrocardiogram usually shows a monophasic Q wave and conspicuous and rather persistent elevation of the Q T segment over the aneurysm while the main QRS deflection is often upright in lead $V_R$ (Goldberger and Schwartz 1948) (fig 15 25) If rupture does not occur during the first few weeks the prognosis is little if at all influenced by the aneurysm (Mover and Hiller 1951)

Fig 15 25 Monophasic Q waves and persistent elevation of the S T segment in all chest leads in a case of left ventricular aneurysm

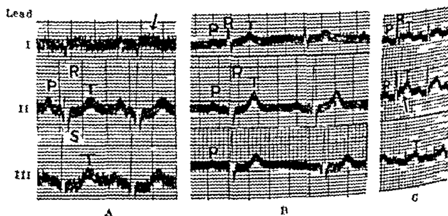



Fig 15 26 —Cardiac infarction complicated by perforation and hæmopericardium.
A Original anterior cardiac infarct n
B After recovery
C After perforation of infarct (hæmopericardium)

*Pericarditis* may be of three kinds (1) a transient friction rub may be heard over an anterior apical infarct and represents a local pericardial reaction (2) there may be widespread pericarditis with friction heard at all areas or at a distance from the lesion which may complicate either anterior or posterior infarcts (3) there may be hæmopericardium resulting from ventricular perforation Local pericarditis does not alter the electro cardiographic pattern of infarction but widespread pericarditis may do so and hæmopericardium invariably does (fig 15 26) Pericardial friction of one kind or another is heard in about 10 per cent of cases

*After effects* The subsequent course is determined by the effect of the occlusion on the total coronary circulation and the amount of healthy muscle left Angina pectoris may develop or if it was present before it may be worse on the other hand if previous pain was due to local ischæmia at the site of the recent infarct angina may improve or temporarily disappear Left ventricular or congestive heart failure may develop during convalescence or subsequently and may cause the disappearance of angina Later cardiac rupture is rare and usually denotes fresh coronary occlusion Less than 10 per cent of ruptured hearts are due to an old ventricular aneurysm (Munck 1946)

## *DIFFERENTIAL DIAGNOSIS*

In the differential diagnosi of myocardial infarction, many conditions must be borne in mind the most confusing are massive pulmonary embolism acute pericarditis dissecting aneurysm of the aorta diaphragmatic hernia œsophageal or gastric dysfunction and acute pancreatitis but diaphragmatic pleurisy especially when bilateral disease of the gall bladder perforated duodenal ulcer epidemic myalgia and pain referred from the spine may give rise to difficulty In *pulmonary embolism* the most important clue is early engorgement of the cervical veins and immediate hypotension whilst rhythm changes are very rare otherwise both symptoms and signs may be indistinguishable from those of coronary thrombosis and even limb lead electrocardiograms may resemble those of posterior cardiac infarction Fortunately however chest lead graphs are diagnostic (page 813) *Acute pericarditis* may simulate cardiac infarction closely but may be distinguished by the electrocardiogram (page 658) *Dissecting aneurysm* is characterised by radiation of pain to the back and downwards by hypertension by the absence of electrocardiographic change by the development of aortic incompetence and perhaps by signs of involvement of carotid subclavian renal or femoral arteries (page 924) *Diaphragmatic hernia* should be considered when there are no changes in temperature white count E S R and electrocardiogram and may be diagnosed by means of a barium meal with the patient in the head down position *Œsophageal or gastric pain* may be felt in the centre of the chest and may resemble the pain of cardiac infarction but physical examinati

is entirely negative the electrocardiogram remains normal and the subsequent course is benign *Acute pancreatitis* may be recognised by the urinary diastase test

## TREATMENT

Patients should be *confined to bed* at once and should remain there for three to six weeks or longer according to the severity of the illness and to the behaviour of the sedimentation rate and electrocardiogram If the blood pressure is low and the patient faint or dizzy he may have to lie flat otherwise and particularly if there is any sign of failure he should be propped up against a back rest in order to reduce the work of the heart

*Semi starvation* for the first few days followed by an 800 calorie diet during the dangerous period practically halves the mortality rate (Master *et al* 1936) Fruit drinks and soft stewed or fresh fruit with sugar and a little milk is all that should be allowed for the first forty eight hours The quality of the later light diet matters less than its bulk and calorific value but should contain little sodium if there is any evidence of failure and little fat

The most beneficial drug in the acute phase is *morphine* which should be given in adequate doses and as often as required to relieve pain and distress and to induce rest and sleep Excellent results are obtained when pain is severe by giving it intravenously in a dose not exceeding ¼ of a grain (15 mg ) dissolved in at least 2 ml of sterile water or saline and at a slow rate three minutes being taken over the injection *Pethidine* 50 to 100 mg by mouth may be taken subsequently at four to six hourly intervals if necessary

*Quinidine* 3 to 5 grains (0 25 G ) t d s has been given in the hope of preventing ventricular fibrillation and other changes of rhythm but with little success (Cutts and Rapoport 1952) although it prevents ventricular fibrillation in dogs (Wegria and Nickerson 1943)

*Heparin* and certain prothrombin inhibitors such as dicoumarol tromexan (ethyl biscoumacetate) and dindevan (phenylindanedione) have been used widely in recent years to prevent extension of coronary thrombosis mural thrombosis and phlebothrombosis

Heparin 15 000 units should be given intravenously at once followed by 15 000 units intramuscularly or subcutaneously eight hourly during the first two days Dindevan should also be given as soon as possible starting with 150 mg on the first day 100 mg on the second and 50 mg on the morning of the third subsequent doses being regulated according to the prothrombin time which should be maintained at two and a half times the prothrombin time in a normal control i e at a ratio of 2 5 The treatment should be started at once in the patient s home for laboratory control is unnecessary until the third day

The results of such treatment in 432 cases were compared with those of conservative management in 368 controls by a special committee of the American Heart Association and were reported by Wright Marple and Beck (1948) The chief findings were as follows

| | Controls per cent | Cases treated with anticoagulants per cent |
|---|---|---|
| Mortality | 24 | 15 |
| Thrombo embolic deaths | 10 | 3 |
| Thrombo embolic complications | 25 | 11 |

Very similar figures for 301 cases treated with anticoagulants and 160 controls were published by Kerwin (1953) in the treated group the mortality was 17 9 per cent and the incidence of thrombo embolic complications 7 6 per cent in the control series the mortality was 29 4 per cent and the incidence of thrombo embolic complications 20 per cent In Great Britain the results of anticoagulant therapy have been much the same Gilchrist and Tulloch (1954) for instance treated 321 cases over a period of seven years and claimed to have halved the mortality rate

Considering the uniformity of published results of anticoagulant therapy it is remarkable that many critical observers still feel uneasy about their reliability (e g Evans 1954) The difficulty in accepting the figures arises from the disbelief that drugs like dicoumarol tromexan and dindevan could diminish the mortality from ventricular fibrillation shock cardiac rupture and heart failure which together should be responsible for the great majority of deaths Prior to anticoagulant treatment deaths from pulmonary and systemic embolism were put no higher than 5 per cent so that allowing for a five fold decrease in thrombo embolic mortality (Wright Marple and Beck 1954) it is still difficult to see why the total death rate should fall more than 4 per cent It is possible however that extension of coronary thrombosis is a more important cause of disaster than at present believed and that anticoagulants tend to prevent this Of 95 deaths from cardiac infarction analysed by Selzer (1948) for instance five were attributed to secondary coronary thrombosis Both heparin and dicoumarol also appear to be coronary vasodilators (Gilbert and Nalefski 1949) and may therefore improve the total coronary flow

According to Schnur (1953) and Russek and Zohman (1954) the risk of serious hæmorrhage (1 per cent) does not justify the use of anticoagulants in mild cases for in these the natural mortality is only 3 per cent, and the frequency of thrombo embolism 0 8 per cent By mild is meant a first attack absence of shock disappearance of severe pain within a few hours normal rhythm absence of heart failure absence of gallop rhythm no cardiac enlargement and no diabetes Against this attitude may be set

negligible risk of hæmorrhage when dindevan is used and when good laboratory facilities are available, and the disastrous consequences that may follow extension of the thrombosis

Permanent anticoagulant treatment to prevent further attack of coronary thrombosis is under trial (Nichol and Borg 1950) An encouraging report comes from Suzman Ruskin and Goldberg (1955) who treated 82 cases continuously over periods ranging between three month and six years Comparing the results with those of 88 untreated control observed over the same period they found the mortality was reduced from 33 to 7 3 per cent and the frequency of recurrences of coronary thrombosis from 24 to 7 per cent When severe cases only were considered (67 cases) the mortality was still only 9 per cent in the treated group, compared with 46 7 per cent in 60 untreated controls and the frequency of recurrences 7 per cent against 21 per cent in the controls Owren (1954) treated 128 cases of uncomplicated angina pectoris with dicoumarol or dindevan for one to five years coronary thrombosis occurred in ten instances during this period and the mortality during the first year of treatment was 5 per cent of 108 patients who had had one previous attack of cardiac infarction seven developed a second coronary thrombosis during the same one to five year period of anticoagulent treatment These results compare favourably with the natural course of ischæmic heart disease

The *coronary vasodilators* with the possible exception of aminophylline do not relieve the pain of cardiac infarction and do not influence its course aminophylline may perhaps improve the collateral circulation and may help to prevent cardiac asthma

*Oxygen* may be given in severe cases but is not routine therapy in Great Britain There may be some advantage in supersaturating the arterial blood particularly when respiration is depressed spontaneously or as a result of morphine

*Cortisone* has been said to halve the mortality from experimental cardiac infarction in animals (Johnson *et al* 1953) moreover infarcts produced in the treated animals were found to be far smaller than in the control Healing however was delayed and fibroblastic proliferation much decreased Opdyke (1953) on the other hand found no diminution in the size of experimentally induced infarcts in cortisone treated animals

*Treatment of complications*

*Shock* has been treated actively in recent years and its mortality has been reduced from 80 to 50 per cent Blood transfusion was tried (Epstein and Relman 1949) but soon abandoned, and intra arterial infusion proved no better (Berman *et al* 1952) but encouraging results have been obtained with vasopressor drugs such as mephentermine noradrenaline and aramine

Mephentermine (wyamine) may be given intramuscularly in a dose of 30 to 40 mg, and repeated when necessary or intravenously at the rate

of 1 mg per minute until the blood pressure is 120 mm Hg which is usually reached in 5 to 20 minutes (Hellerstein Brofman and Caskey 1952)

Noradrenaline or L noradrenaline (levophed) 10 mg. dissolved in a litre of 5 per cent glucose solution may be given by intravenous drip infusion at the rate of 10 to 20 drops per minute each ml (15 drops) of the solution contains 10μg of noradrenaline The rate of infusion should be regulated to maintain the blood pressure at 120 mm Hg and continued as long as necessary (up to 72 hours) In England Shirley Smith and Guz (1953) reported encouraging results with this treatment In the United States Griffiths *et al* (1954) reduced the mortality of shocked cases from 80 to 47 8 per cent prior to the treatment 128 out of 161 shocked patients died in their series of 816 proved cases of acute coronary thrombosis since starting treatment with pressor amines 64 out of 134 shocked cases died and when treatment was begun within three hours of the onset only 13 per cent died These figures are impressive

Aramine in doses of 0 01 to 0 1 mg per kilo body weight improves cardiac function and coronary blood flow while maintaining the blood pressure in cardiogenic shock (Sarnoff *et al* 1954) It may be given orally intramuscularly or by drip infusion (0 1 to 0 5 mg per minute)

Since appreciating that shock in acute cardiac infarction is a form of acute heart failure it is rational to try digitalis Gorlin and Robin (1955) reported good results with lanatoside C or Ouabain intravenously in four cases although they used very small doses (0 4 mg of lanatoside C and 0 05 to 0 2 mg of Ouabain) This lead should be followed up

*Conventional heart failure* usually responds well to routine treatment with posture a low sodium diet mercurial diuretics and digitalis The danger of the digitalis glycosides (Travell Gold and Modell 1938) should not be over emphasised and they must not be withheld when the need for them arises

*Serious disturbances of rhythm* call for their standard treatment Ventricular tachycardia can usually be controlled with adequate doses of quinidine or procaine amide atrial fibrillation flutter or tachycardia with digitalis heart block with ephedrine Under the appropriate circumstances these drugs may have to be used boldly without fear that they may cause cardiac standstill or ventricular fibrillation in the presence of cardiac infarction

*The frozen shoulder syndrome* (left) that can prove troublesome for months after cardiac infarction may often be relieved by cortisone according to Russek *et al* (1953) Hydrocortisone 50 mg in a 2 ml. suspension with the addition of 1 000 units of hyaluronidase and 2 ml. of 2 per cent procaine may be injected weekly into the subacromial bursa anteriorly into the long head of the biceps antero laterally and into the joint capsule posteriorly as described by Crisp and Kendall (1955)

*Subsequent management*

If the course is benign and the patient looks and feels well, he may be allowed up after three weeks provided the sedimentation rate has returned to normal and the electrocardiogram does not show a large infarct Most cases require a month in bed and a further fortnight resting at home on a couch but those with complications should remain in bed for six weeks or longer

Six weeks to three months convalescence is usually needed while the patient regains his confidence and gradually resumes his ordinary activities Radical change of employment is rarely practicable in this age group but lighter work and less responsibility may have to be advised Relatively good recovery from the first attack is the rule, but severe angina or recurrent congestive failure may cause total incapacity after second or third attacks

## PROGNOSIS

With conservative treatment the mortality during the first month of acute cardiac infarction is 25 per cent This figure is based on 3 948 cases collected from ten unselected series in the literature mostly first attacks and does not take into account all those cases that failed to survive long enough to receive skilled medical attention and hospital care The mortality was also 25 per cent for 2 733 first attacks only for second and third attacks it is said to be higher Doscher and Poindexter (1950) found a combined mortality rate of 23 5 per cent in over 4 000 cases in the literature

When assessing the influence of any new therapy on the mortality rate of acute cardiac infarction many factors must be taken into consideration

1 First attacks are believed to have a lower mortality than subsequent attacks assuming (possibly without justification) that abrupt death at the onset is not more frequent in first attacks

2 Four fifths of all deaths from acute cardiac infarction occur in the first twenty four hours 60 per cent in the first two hours and 50 per cent within the first fifteen minutes at least in men under 40 years of age having their first attack (Yater *et al* 1948)

3 The mortality in women averages 50 per cent higher than in men (Mintz and Katz 1947 Doscher and Poindexter 1950)

4 Mortality in men is proportional to age in a group of 276 cases studied by Fitzgerald Peel (1955) it ranged from 5 per cent in men under 44 years old to 35 per cent in men over 65 in women it was 25 per cent at all ages

5 The following complications adversely influence the mortality which is given in brackets when known complete heart block (80–90 per cent) shock (75–80 per cent) paroxysmal tachycardia of any type or atrial flutter (66 per cent) pneumonia (57 per cent) left ventricular or congestive heart failure (50 per cent) gallop rhythm a pulse pressure under 20 mm. Hg

a blood pressure under 90 mm Hg bundle branch block unquestionable cardiac enlargement intractable pain diabetes mellitus and marked obesity (Mintz and Katz 1947 Russek and Zohman 1952)

6 The following factors do not influence the mortality rate previous angina pectoris previous hypertension absence of pain the site of the infarct ectopic beats and pericarditis (Mintz and Katz 1947)

7 The mortality in favourable cases without any of the adverse features listed above is only 3 to 5 per cent and the incidence of thrombo embolism in this group is only 1 to 3 per cent (Russek and Zohman 1952 1954)

8 Particularly favourable are those cases with electrocardiograms that show simple inversion of the T wave only without pathological Q waves and without initial elevation of the RS T segment (East and Oram 1948 Papp and Smith 1951 Holzman 1955) especially when there is no significant fever leucocytosis or rise of sedimentation rate (Helander 1950)

*Mortality of specially treated cases*

With prompt skilled medical and nursing attention early intravenous heparin proper use of vasopressor drugs within three hours of the onset of shock a semi starvation diet (800 calories approximately) containing not more than 0 5 G of sodium for the first few days prothrombin inhibitors for four to six weeks either in all cases or at least in those with one or more unfavourable features early recognition and efficient treat ment of left ventricular or congestive heart failure immediate antibiotic therapy for complicating pneumonia good control of diabetes mellitus and the intelligent treatment of serious changes of rhythm the natural mortality of 25 per cent in all cases that survive the first fifteen minutes of the attack should be reduced to about 10 per cent

*Ultimate prognosis*

Of patients who survive the first acute attack of cardiac infarction about a third make a complete functional recovery 50 per cent have angina pectoris or limited cardiac reserve but are able to lead useful lives and 20 per cent are seriously incapacitated with severe angina or heart failure (Mussafia and Masini 1948 Master and Jaffe 1951 Cole Singian and Katz 1954) If the ultimate prognosis of any particular case is to be based on statistical evidence these three groups must be considered separately

Patients with good functional recovery are not only free from angina pectoris but are also able to increase their cardiac output normally on effort (Chapman and Fraser 1954) About 90 per cent of such patients survive five years and 70 per cent ten years (Master and Jaffe 1951 Cole et al 1954)

Of the patients with mild or moderate angina pectoris about three quarters survive five years and one half survive ten years (Cole et al 1954)

In the severe group, however the majority die within five years

The crude average life expectation following recovery from the first attack of cardiac infarction is about eight years The chief causes of death include fresh cardiac infarction (66 per cent) and heart failure (20 per cent) (Katz *et al*, 1949)

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CHAPTER XVI

# HYPERTENSIVE HEART DISEASE

HYPERTENSIVE heart disease is but one facet of the whole problem of systemic hypertension It is necessary to consider this problem first

## DEFINITION

Hypertension implies elevation of the basal blood pressure above the arbitrary normal limits of 145/90 mm Hg Physiological vasoconstriction or a transient increase of cardiac output due to emotion cold or other trivial cause is common and modifies the significance of casual high readings of the order of 160/90 mm Hg The basal pressure is that obtained when the subject is lying down and when successive readings at five minute intervals have dropped to a steady level If there were an easy bedside method of measuring the cardiac output hypertension would be expressed in terms of total peripheral resistance In healthy young adults

$$\text{R (resistance)} = \frac{\text{80 to 100 mm Hg (mean arterial pressure)}}{\text{5 to 8 L/min (cardiac output)}}$$
$$= \text{10 to 20 units}$$
$$= \text{800 to 1 600 dynes sec /cm}^5 \text{ (page 177)}$$

Unquestionable hypertension means a peripheral resistance above 25 units (2 000 dynes sec /cm $^5$) It is insufficiently realised that with an average peripheral resistance of 15 units a cardiac output of 10 litres per minute which is common in mildly excited young adults would raise the blood pressure to around 210/110 mm Hg (mean 150 mm Hg) With a relatively high normal resistance of 18 units and a cardiac output of 12 litres per minute resulting from more marked excitement (also common enough) the physiology of the circulation could still be normal with a blood pressure of 300/150 mm Hg (mean 210) That such hyperkinetic levels are not commonly encountered in healthy but apprehensive young adults is due to the fact that when the cardiac output rises in response to adrenergic stimuli the peripheral resistance falls The figures given however should serve to emphasise the fact that measurement of the blood pressure without reference to the cardiac output provides no evidence of the state of vasomotor tone and is therefore a poor method of detecting essential hypertension or of estimating its degree Once this is understood many of the anomalies that surround the height of the blood pressure in normal hypertensive subjects fall into line *Hyperkinetic elevation of the pressure is not essential hypertension*

When elevation of the blood pressure shows disproportion between systolic and diastolic levels, systolic bias favours rigidity of the aorta and large vessels as in atherosclerosis or increased force of cardiac contraction as in thyrotoxicosis whereas diastolic bias favours vasoconstriction, as in true hypertension

## VARIETIES OF HYPERTENSION

Hypertension may be paroxysmal, as in phæochromocytoma of the adrenal medulla transient, as in acute nephritis and toxæmia of pregnancy or persistent, as in chronic nephritis chronic pyelonephritis surgical kidney coarctation of the aorta Cushing s syndrome and essential and malignant hypertension High blood pressure accompanying thyrotoxicosis and the climacteric is coincidental statistical analysis shows no significant *correlation and the pressure does not fall when these disorders are* corrected (Bechgaard 1946) The blood pressure in obese subjects may appear to be higher than it really is owing to the unreliability of the cuff method of measurement when applied to a fat limb lower pressures may be recorded by direct arterial puncture Under certain conditions e g during a rigor when there is intense vasoconstriction or when the main artery to the limb is partly occluded, the blood pressure reading may be *much lower when measured by the cuff method than when measured by* direct arterial puncture indeed it may be immeasurable by ordinary means when direct puncture proves it to be in the region of 100 mm Hg Such fallacies must be constantly borne in mind Hypertension associated with mitral stenosis is almost certainly a matter of chance apart from the transient rise of pressure that may result from heart failure

## INCIDENCE

In 1928 hypertension accounted for 14 8 per cent (Bell and Clawson) to 20 per cent (Fahr) of all deaths in the U S A in people over 50 years of age *In England and Wales the Registrar General s Statistical Review for* 1953 reveals that 4 per cent of all deaths (8 per cent of cardiovascular deaths) were due to hypertension and another 13 5 per cent of all deaths *(27 per cent of cardiovascular deaths) to stroke chiefly cerebral hæmorrhage* or thrombosis

If a blood pressure of 150/100 mm Hg or above means hypertension then the prevalence of this disease is 5 per cent *in young adults* 10 to 20 per cent in the fifth decade 20 to 30 per cent in the sixth decade and 35 to 40 per cent in those between the ages of 60 and 65 (Master *et al* 1952) As pointed out by Hamilton *et al* (1954) there *is no sharp dividing* line between what is normal and what is abnormal If 180/105 mm Hg is accepted as the lower limit of genuine hypertensive disease then its prevalence is 0 7 per cent in young adults under 40 years of age 3 per cent *in the fourth decade 6 per cent in the fifth decade* and 10 per cent between the ages of 60 and 65 (Master *et al* 1952) Males are more prone to

hypertension than females up to the age of 40, but thereafter it is the other way about

At least 80 per cent of hypertensive subjects are between 40 and 70 years of age the peak period being 50 to 59 (Janeway 1913 Bechgaard 1946) According to Platt (1948) severe persistent hypertension in persons under 40 years of age is commonly renal less than a third of his series were essential and he encountered no primary malignant cases under the age of 34

The sex incidence is about equal men being rather more frequently affected in the upper classes (Janeway 1913 Ehrstrom 1918) women in the lower (Blackford *et al* 1930 Bechgaard 1946) Malignant hyper tension however affects three men to one woman

About 80 to 85 per cent of cases of persistent hypertension are essential about 2 per cent are primary malignant and most of the remainder are renal Brod (1955) found a particularly high incidence of malignant hyper tension amongst his cases of chronic pyelonephritis (20 per cent)

High blood pressure appears to be linked with civilisation it is said to be rare or uncommon in China amongst orientals generally (Harris 1927) and in negroes (Donnison 1929) but it is as common or more common in civilised negroes in the U S A as in the white population (Fishberg 1939) The evidence has been reviewed by Smirk (1949)

## PATHOGENESIS

*Paroxysmal hypertension* is due to an excess of circulating adrenaline released by a phæochromocytoma of the adrenal medulla (Beer King and Prinzmetal 1937) it is now known that there is also an excess of nor adrenaline sometimes one and sometimes the other predominating (Pitcairn and Youmans 1950)

*Transient hypertension in acute nephritis* appears to depend upon a ner vous rather than a humoral agent (Pickering 1943) and may be due to extra renal factors (Kylin 1926) There is reason to believe that acute nephritis is an allergic vascular reaction to the products of remote bacterial infection (Cavelti and Cavelti 1945) usually but not exclusively strepto coccal the brunt of the attack falling on the glomerular tufts but the capillaries elsewhere not escaping entirely General vasospasm may cause the hypertension Wilson (1953) on the other hand accepts the obvious and assumes that the hypertension of acute nephritis is renal and humoral in origin

Hypertension in *toxæmia of pregnancy* may be transient and behave like that in acute nephritis or it may be persistent and resemble essential or malignant hypertension (Golden Dexter and Weiss 1943) Since the blood volume and cardiac output are raised the hypertension may be partly hyperkinetic More measurements of the peripheral resistance in toxæmia of pregnancy are needed

High blood pressure in *coarctation of the aorta* (page 332) probabl

results from diminution of the renal blood flow It does not occur experimentally if the aorta is constricted below the origin of the renal arteries (Rytand 1938)

Hypertension resulting from *chronic nephritis, chronic pyelonephritis* (Schoen 1930 Longcope and Winkenwerder 1933) and certain *surgical kidneys* (Braasch Walters and Hammer 1940) is almost certainly attributable to a humoral agent liberated by the diseased kidney (Pickering 1943) at least in the first instance

*Malignant hypertension* may develop in any form of hypertension provided the diastolic blood pressure rises sufficiently particularly when it does so rapidly (Pickering 1952)

## ETIOLOGY OF ESSENTIAL HYPERTENSION

Certain predisposing factors must be considered first

*Heredity* According to Platt (1947) essential hypertension could be a hereditary disease conveyed as a Mendelian dominant with a rate of expression of more than 90 per cent This may be an extreme view but the importance of the hereditary factor cannot be denied Thus Ayman (1934) studying 277 families found hypertension in the children in 3 1 per cent of the families when both parents were normal in 28 3 per cent when one parent was hypertensive and in 45 5 per cent when both parents were hypertensive Again in an investigation based upon 256 members of 50 families Hines (1940) found that the children were hyper reactors to the cold pressor test in 43 4 per cent when one parent was either hypertensive or a hyper reactor and in 95 per cent when both parents were affected In Bechgaard s series of over 1 000 cases of persistent hypertension which included 20 7 per cent possible renal cases (*in which there is no hereditary factor*) one or both parents were seriously hypertensive in 75 per cent

*Hyper reaction to pressor agents* The excessive reaction of hypertensive subjects to the cold pressor test of Hines (1940) is the best example. The test is carried out as follows the basal blood pressure is first recorded in the usual way the subject s free hand is then plunged into ice cold water (3° to 5 C) to just above the level of the wrist and immersed for one minute while the blood pressure is recorded at half minute interval In 85 per cent of normal persons the blood pressure rises an average of 12 4/10 1 mm Hg and returns to its previous level within two minutes If the immersed limb is anæsthetic there is no response whether the anæsthetic is organic or hysterical (Wolff 1951) A rise of more than 20/15 mm Hg is regarded as a hyper reaction Patients with established essential hypertension show an average rise of 46 6/30 9 mm Hg 95 per cent being hyper reactors Follow up studies indicate that apparently normal individuals who are hyper sensitive to the cold pressor test are likely to develop persistent hypertension Hines also claims that high casual readings due to emotion have the same significance and Harris *et al* (1951)

agree but this is not substantiated by the subsequent histories of patients with Da Costa s syndrome (Grant 1925 Wood 1941)

Holding the breath for 20 seconds may also be used as a pressor agent in much the same way, and compares favourably with the cold pressor test (Ayman and Goldshine 1939)

*Other factors* The influence of civilisation and of sex in malignant hypertension have already been mentioned

*Structural changes in the vessels* Certain structural vascular changes often found associated with hypertension have been proved to play no part in its production Atherosclerosis is innocent in this respect unless a plaque constricts the renal artery increased rigidity of the aorta and great vessels may raise the systolic pressure increase the pulse volume and accelerate the speed of the pulse wave but it has little influence upon the mean blood pressure Calcification of the media of medium sized arteries has a similar effect The characteristic vascular lesion which is the signature of malignant hypertension necrosing afferent glomerular arteriolitis is a result not a cause of extreme hypertension Multiplication of the internal elastic lamina and hypertrophy of the media of small arteries and arterioles are also effects not causes of sustained hypertension Hyaline thickening of the intima especially of the afferent glomerular arteriole found in 98 per cent of cases of essential hypertension is the only vascular lesion possibly to blame which has not yet been proved to be a result of high blood pressure (Pickering 1943)

*Experimental studies* The classical experiments of Goldblatt (1934 *et seq*) proved that persistent hypertension could be induced in dogs by constricting both renal arteries unilateral constriction failed unless the other kidney was removed Hypertensive retinopathy and wide-spread arteriolar necrosis similar to malignant hypertension in man were reproduced by more severe constriction but the renal vessels distal to the clamp were spared Similar results were obtained in rabbits by Wilson and Pickering (1937) In 1939 Wilson and Byrom succeeded in causing persistent hypertension benign or malignant, in rats by constricting only one renal artery The vessels in the other kidney then showed changes comparable in all respects to those seen in benign or malignant hypertension in man

The conclusion that the difference between essential and malignant hypertension is merely one of degree is supported by the occasional development of malignant changes in practically all varieties of hypertension including paroxysmal, transient and renal hypertension moreover in the early malignant stage renal biopsy usually reveals no evidence of arteriolar necrosis indicating that this is not an essential part of the picture, but merely a late consequence (Castleman and Smithwick 1943)

*Biochemical hypothesis concerning the cause of hypertension* Experimental hypertension of the kind just described is believed to depend upon the liberation of an excess of renin by the ischæmic kidney Renin combines with an enzyme hypertensinogen which is a normal constituent of the

plasma globulins, to form a pressor substance hypertensin or angiotonin (Braun Menendez *et al* 1939) Hypertensin is said to be destroyed by another enzyme hypertensinase (Pickering 1943)

There is as yet, no direct proof that essential hypertension in man is caused by this mechanism although it seems to explain renal hypertension It may also explain rare cases of hypertension associated with atherosclerotic obstruction of one or both renal arteries (Yuile 1944) It should be noted that unilateral renal disease is capable of causing hypertension in man, in other words man behaves like the rat in this respect, not like the dog or rabbit

*Physiology of the circulation in essential hypertension* In essential hypertension vasoconstriction affects chiefly the efferent glomerular arterioles of the kidney the intraglomerular pressure being raised and the cortical blood flow diminished, obviously if the latter were due to vasoconstriction proximal to the glomeruli the intraglomerular pressure would be lowered Blood appears to be diverted from the renal cortex into other channels The classical studies of Trueta and his colleagues (1947) make it highly probable that the juxta medullary by pass provides the principal diversion The vessels of the skin and brain are constricted more or less sufficiently to prevent an increased blood flow through these territories on the other hand the arterioles in skeletal muscle and probably in the heart are little if at all constricted so that they may passively yield to the raised pressure and take some of the shunt The behaviour of the splanchnic vessels remains to be investigated but in normal subjects their reactions tend to be opposite to those in the skin (Grayson 1950) The cardiac output blood volume and blood viscosity are normal Vasoconstriction appears to be humoral rather than nervous in mechanism (Pickering 1945) Hypertensin causes a similar type of vasoconstriction the chief effect is on the efferent glomerular arterioles the skin is involved only to the extent of preventing secondary increase of blood flow the skeletal muscles take some of the shunt That hypertensin is the humoral cause of essential hypertension is therefore an attractive hypothesis (Pickering remarks that the brain and heart being two of the most important organs in the body are provided with special pressor mechanisms the carotid sinus and aortic arch which respond to falling intravascular pressure by causing vasoconstriction as the nature of these organs demands that appropriate adjustments are immediately executed it is natural that the mechanism of this vasoconstriction is nervous But the kidneys are just as vital and it would therefore harmonise with general principles if they too were provided with a pressor mechanism to ensure adequate intraglomerular pressure without which filtration would cease but there is no necessity for sudden adjustments but rather for prolonged ones A humoral mechanism would meet the requirements nicely)

Nevertheless as previously stated proof that essential hypertension in man is due to excessive liberation of renin is lacking Transfusion experi

ments have failed to demonstrate a pressor agent in the venous blood of hypertensive subjects and Light and I (1939) failed to demonstrate a pressor agent in a pint of blood taken from the renal vein of a patient with malignant hypertension and transfused into a boy of nine Even if the humoral mechanism were proved to be the renin hypertensin system we should still be ignorant of the cause of its hyperactivity

A promising line of investigation seems to be that opened up by Trueta and his colleagues at Oxford They have shown that blood reaching the kidney has two alternative routes (1) through the glomeruli of the cortex (2) through a juxta medullary by pass Blood may be diverted from the cortex in varying degree as a result of emotion shock crushing injuries hæmorrhages certain drugs certain bacterial toxins and probably by innumerable other agents In cases of Bright s disease they have noticed degenerative changes in the juxta medullary glomeruli consistent with constant operation of the shunt The significance of these findings will not be overlooked particularly *their suggestion that the juxta medullary* by pass may act as a functional Goldblatt clamp

It is possible that the cause of essential hypertension is simply physiological hypertension repeated too often or sustained for too long a period, as suggested by Smirk (1949) Whether repetitive physiological hyper tension is chiefly hyperkinetic neurogenic (vasoconstrictive) or humoral (vasoconstrictive) is immaterial to this hypothesis which holds that a raised blood pressure however produced may initiate secondary reactions *which themselves* increase the total peripheral resistance and so perpetuate the hypertension Agents capable of causing sufficiently repetitive or prolonged hypertension to excite these secondary changes include a par ticular type of personality that over reacts to stress (hereditary factor) prolonged emotional strain (psychological factor) acute nephritis tox æmia of pregnancy paroxysmal hypertension from phæochromocytoma and certain hyperkinetic circulatory states such as thyrotoxicosis Second *ary changes that* may perpetuate the hypertension are renal ischæmia and arteriosclerosis in its broadest sense, but a more important unknown factor *is postulated* A similar hypothesis has been put forward to explain pul *monary hypertension* for sustained pulmonary vasoconstriction also seems to result from pulmonary hypertension *however caused* (page 839)

## CLINICAL FEATURES

### *PAROXYSMAL HYPERTENSION*

Paroxysmal hypertension first described by Frankel (1886) is rare being responsible for only *0 5 per cent of* cases of severe persistent hyper tension (Graham 1951) It usually *occurs in* youthful or early middle aged subjects of either sex and is characterised by recurrent attacks of pal pitation headache and vomiting *angina* pectoris or even acute pulmonary œdema (Howard and Barker 1937) may be associated Abdominal com

pression as occurs on stooping may provoke an attack but usually there is no previous precipitating cause During the crisis, which may last for minutes or hours, the blood pressure (systolic and diastolic) is extremely high most of the skin is cold, pale and mottled but the forehead, face and neck may be flushed Sweating and trembling may follow Between attacks the patient is usually well but persistent hypertension occasionally malignant, develops sooner or later in the majority (Green 1946)

The quality of the symptoms depends upon whether the tumour liberates chiefly adrenaline or noradrenaline although both are usually present in excess Adrenaline is the body s emergency hormone and is normally released by the suprarenal medulla in amounts proportional to physiological estimates (Cannon 1940) It increases the heart rate venous pressure (Iglauer and Altschule 1940) and strength of cardiac contraction (Marsh *et al* 1948) so that the cardiac output is increased by means of all three reserve mechanisms (McMichael and Sharpey Schafer 1944 Goldenberg *et al* 1948) while the coronary blood flow is augmented (Anrep and Stacey 1927) and the total peripheral resistance diminished (von Euler and Liljestrand 1927) Although the blood flow through the skin (Barcroft and Swan 1953) and through the kidneys (Barclay Cooke and Kenney 1947) is reduced the blood flow through skeletal muscle (Allen Barcroft and Edholm 1946) and liver (Bearn Billing and Sherlock 1952) is greatly increased Adrenaline also stimulates all impulse forming foci in the heart whether normal or abnormal The chief clinical effects of an excess of circulating adrenaline are therefore pallor of the skin tachycardia abnormalities of rhythm a bounding pulse marked elevation of the systolic but less of the diastolic blood pressure (hyperkinetic hypertension) and a hyperdynamic heart action the chief symptoms are palpitations and a sense of alarm

Noradrenaline is liberated physiologically at sympathetic nerve endings where it activates effector cells (von Euler 1946 1948) but it is also found in the adrenal medulla where it forms up to 25 per cent of the total secretion (Swan 1952) Noradrenaline is a powerful vasoconstrictor of all but the coronary vessels and causes a sharp rise of systolic and diastolic blood pressures and of total peripheral resistance The pulse rate slows reflexly owing to stimulation of carotid and aortic baroreceptors and though the stroke volume and power of ventricular contraction may be enhanced the minute output does not rise (Goldenberg *et al* 1948) Noradrenaline does not stimulate impulse forming foci in the heart and does not encourage changes of rhythm (Nathanson and Miller 195 ) The chief clinical effects of an excess of circulating noradrenaline are therefore pallor, systolic and diastolic hypertension, and bradycardia

Mixtures of adrenaline and noradrenaline (arterenol) infused at the rate of 10 μg per minute behave like adrenaline when there is less than 25 per cent of noradrenaline in the mixture (as in normal medullary secretion) with adrenaline/noradrenaline ratios of 3/1 to 1/3 the adrenaline effec

still predominate but with ratios of 1/8 or less the noradrenaline effects predominate balanced effects are observed with ratios between 1/3 and 1/8 (De Largy *et al* 1950)

A mass about the size of an orange may be felt in the abdomen in one third of the cases or may be demonstrated by simple skiagrams pyelograms or other radiological methods. The adrenal medullary tumour is commonly unilateral and benign There is usually a considerable excess of circulating adrenaline or nor adrenaline all the time and in attacks there may be a thousand times the normal quantity (Mackeith 1944) The electrocardiogram may show the usual pattern associated with persistent hypertension or it may show evidence of acute left ventricular stress during attacks—inversion of the T wave in leads facing the surface of the left ventricle

Death may result from cerebral hæmorrhage acute pulmonary œdema or ventricular fibrillation

Following the demonstration by Clerc and Sterne (1937) that a synthetic benzodioxan (diethyl aminoethyl benzodioxan) in oral doses of 0 05 G six hourly relieved all symptoms immediately and prevented further attacks the administration of this substance has been used as a diagnostic test for the condition (Goldenberg *et al* 1947 Cahill 1948) The usual dose is 0 25 mg per kilogram body weight intravenously In cases of phæochromocytoma the systolic and diastolic blood pressures drop sharply for 10 to 15 minutes whereas in other forms of hypertension they tend to rise a little sometimes alarmingly so

Of the newer adrenolytic drugs such as dibenamine (3 to 5 mg /Kg intravenously) dibenyline or dibenzyline (0 25 to 0 5 mg /Kg intravenously or 20 to 50 mg three or four times daily orally) rogitine (*vide infra*) and ilidar (25 to 50 mg three or four times daily by mouth) rogitine is probably the most satisfactory for detecting or excluding phæochromocytoma Rogitine (phentolamine) is related to priscoline both being derivatives of amidazoline For diagnostic purposes a dose of 5 mg is given intravenously in cases of phæochromocytoma the blood pressure falls more than 35/25 mm Hg within two or three minutes and then gradually returns to the basal level over the next 10 to 15 minutes (Gifford Roth and Kvale 1952) Dangerous pressor reactions in essential or malignant hypertension, such as may occur with benzodioxane (Rosenheim, 1954) do not seem to occur with phentolamine The drug may also be given orally in doses of 20 mg three or four times daily

A marked fall of blood pressure after intravenous dibenamine dibenzyline or ilidar is not specific for phæochromocytoma for these drugs are all sympatholytic as well as adrenolytic in the doses used whereas phentolamine is not

The intravenous injection of 0.025 mg. of histamine (Roth and Kvale 1945) or of 300 mg of tetraethylammonium bromide is also helpful in diagnosis for in cases of phæochromocytoma both *raise* tl — pressure

(La Due *et al* 1948) Mecholyl may have the same effect but is unreliable (Anderson *et al*, 1952) Hexamethonium (and presumably ansolysen) appears to excite similar responses to those of tetraethyl ammonium (Freis *et al* 1951)

The most reliable test for phæochromocytoma however is to estimate the plasma adrenaline and noradrenaline or the output of these catecholamines in the urine In normal controls and in patients with essential hypertension they should not exceed 2 5 µg per litre in the plasma (mean 1 6), mostly noradrenaline whereas in cases of phæochromocytoma with sustained hypertension and in paroxysmal cases after a test dose of histamine they usually exceed 12 µg per litre adrenaline alone exceeding 4 µg (Manger *et al* 1954) In normal subjects at rest in bed only infinitesimal amounts of adrenaline and noradrenaline are excreted and in subjects leading quiet lives only about 5 µg of adrenaline and 20 to 40 µg of noradrenaline are excreted within 24 hours In cases of phæochromocytoma however up to 100 times this quantity is excreted within 24 hours (Engel and von Euler 1950)

Treatment is surgical and may be entirely successful but the operative mortality is about 30 per cent (Mackeith 1944) The chief dangers are extreme hyper adrenalism during manipulation of the tumour and a profound drop in blood pressure following its removal Dibenyline 20 mg three or four times daily (Allen *et al* 1951) or phentolamine, 20 to 40 mg t d s may be given orally to control the pre operative situation and noradrenaline may be infused post operatively, at a rate of approximately 10 µg per minute to control the transient circulatory collapse that may follow removal of the tumour

## *TRANSIENT HYPERTENSION*

The clinical features of acute nephritis and toxæmia of pregnancy are beyond the scope of this work and their effect upon the heart is discussed elsewhere (page 638)

## *PERSISTENT HYPERTENSION*

It is doubtful whether any symptoms can be ascribed to high blood pressure itself Certainly the majority of cases are discovered accidentally or by reason of complications Headaches fatigue dizziness difficulty in concentration and palpitations are commonly due to anxiety whether the blood pressure is raised or not Redistribution of blood due to selective vasoconstriction may however determine the behaviour of two variables It was stated previously that vasoconstriction in skin and brain was more or less sufficient to prevent an increase of blood flow through these territories as a result of raised pressure the words more or less may now be amplified Thus more cutaneous vasoconstriction may be responsible for the pale hypertensive less for the red more cerebral vasoconstriction may be responsible for dizziness failing memory and for general mental

deterioration less for headache The more important symptoms associated with hypertension are due to cardiac renal or cerebral complications and will be discussed later

*The blood pressure* is necessarily raised a diagnosis of previous persistent hypertension when the blood pressure is found to be normal is nearly always wrong unless there is severe hæmorrhage shock massive pulmonary embolism or myocardial infarction It is customary to recognise four grades of hypertension according to the level of the diastolic pressure between 95 and 110 mm Hg is considered mild 110 to 125 moderate 125 to 140 severe, above 140 gross The systolic pressure may be at any level between 150 and 300 mm Hg and may modify the grade accordingly With mild hypertension it is usually between 150 and 200 with moderate hypertension between 180 and 230 with severe between 210 and 260 with gross between 240 and 300 Essential and nephritic hypertension may be of any grade malignant hypertension is always severe or gross The frequent discrepancy between the grade of hypertension itself and the severity of the disease as a whole is explained by the fact that the blood pressure without reference to the cardiac output is only a rough guide to the total peripheral resistance

*The pulse* is firm and varies considerably in amplitude from case to case In the more severe grades it is apt to be small in those with marked atherosclerosis large If the pulse is full and bounding the raised pressure is more likely to be due to a hyperkinetic circulatory state (high cardiac output) Hard tortuous or calcified peripheral arteries indicate atherosclerosis or Monckeberg s sclerosis not hypertension—although they may be associated In the latter event one or other carotid usually the right may be kinked and then mistaken for an aneurysm or carotid pulsation may be so increased in amplitude as to suggest aortic incompetence A diminished and delayed femoral pulse associated with absent dorsalis pedis and posterior tibial pulses indicates coarctation of the aorta Pulsus alternans may occur in severe cases and is usually associated with heart failure or with ectopic beats

*Retinoscopy* may reveal arterial thickening hæmorrhages exudates or papillœdema (Liebrecht 1859) and should never be omitted There are five signs of arterial thickening (1) increased tortuosity (2) notching pinching or S shaped bending of veins at arterio venous crossings (3) uniform or irregular narrowing of the arterial blood streams owing to reduction in the diameter of the vascular lumina (4) white arterial fringes or thin white lines bordering the red arterial streams representing the thickened white walls of the arteries themselves—they are rarely seen in more than one or two places and then only for a short distance usually on a bend (5) the single white streak, representing a thrombosed artery with an obliterated lumen Occasionally the distal part of such an artery may be patent due to the development of a collateral circulation

By far the most important of these signs is narrowing of the arterial

lumen Normally the apparent width of a retinal artery compared with its accompanying vein is as 5 5 or 4 5 When the artery is thickened this ratio is decreased and may be about 3 5 or less There is no better way *of expressing the average calibre of the retinal arteries than by giving the* approximate arterio venous ratio

In benign hypertension it is rare to find more than notching of veins and narrowing of the arterial lumina white arterial fringes and obliteration of the lumen usually mean nephritic or malignant hypertension

It should perhaps be added that the appearance of the fundal vessels gives little indication of the state of the cerebral vessels the risk of stroke *cannot be assessed from retinoscopy*

*Retinal hæmorrhage* may be superficial, when it is linear or fan shaped in appearance or deep when it resembles a rounded *smudge Both kinds* may be seen in hypertensive retinopathy but the former is more common Hæmorrhages are unusual in essential hypertension and when present are *usually minute They are not uncommon in nephritic hypertension* and almost invariable sooner or later in the malignant type Just what causes these small hæmorrhages is not clear for the capillary blood pressure is normal in hypertension (Ellis and Weiss 1929-30) and in any case healthy *capillaries can withstand astonishingly high pressures* Hæmorrhage secondary to a venous thrombosis at an arterio-venous crossing is more easily understood

*Thrombosis* of a retinal artery or vein usually causes a defect in the visual field of the affected eye and thrombosis of the central artery or vein causes blindness Unfortunately retinal thrombosis is apt to be recurrent

*Retinal exudates* are of four distinct types (1) large hæmorrhages sometimes reveal eccentric soft white cores which may persist after absorption of the blood (2) soft fleecy patches scattered indiscriminately over the *retina are characteristic of malignant hypertension* (3) complete or incomplete star patterns composed of hard whitish particles or dots radiating from the macula may be seen in chronic nephritic *or in malignant hyper*tension (4) in diabetes mellitus, the exudate is wavy sharply cut and scattered, resembling pale yellow confetti Small areas of *retinal degener*ation in old people should not be confused with exudates

When *papillœdema* is added to the signs of hypertensive retinopathy already described malignant hypertension should be diagnosed Conversely malignant hypertension should not be diagnosed in the absence of papillœdema (Ellis 1938) *Although* chronic nephritis may be responsible little is lost by making the other diagnosis for if there is papillœdema the *course of the disease will certainly be malignant* if acute nephritis and toxæmia of pregnancy can be excluded The appearances may be distinguished from those of cerebral tumour by the arterial changes by a macular star figure or by exudates independent of hæmorrhages

Papillœdema is usually associated with a high cerebro spinal fluid pressure but not invariably moreover higher C S F pressures are found

without papilloedema in cases of superior vena cava obstruction Evidence from experimental hypertension in rats suggests that papilloedema is due to cerebral oedema caused by intense vascular spasm and secondary increased capillary permeability (Byrom 1954) Occasionally, progressive blindness occurs

*Examination of the heart* usually reveals some degree of left ventricular hypertrophy The apex beat becomes displaced slightly to the left and downwards the cardiac impulse becomes heaving in quality and unusually easy to feel It is quite different from the short sharp thrust of the overacting heart for it is a quiet unhurried action giving the impression of great strength The hyperdynamic quality of the former may be compared with the first few strokes of a racing crew galvanised into urgent action by the sound of the starting signal the heaving impulse of left ventricular hypertrophy to the powerful steady drive maintained by the crew when it has settled down to a long hard struggle If, with due care, the apex beat cannot be located, left ventricular hypertrophy is unlikely even in obese subjects, unless masked by emphysema

Presystolic gallop rhythm is common with severe hypertension and means that the left ventricle is receiving atrial help to increase its diastolic stretch so that it may contract more powerfully The second sound at the base is accentuated and high pitched Functional aortic incompetence is not uncommon and may be associated with diastolic pressures of 130 to 170 mm Hg in other words it may not affect the circulatory dynamics It is due to dilatation of the aortic ring and may be compared with functional pulmonary incompetence in cases of pulmonary hypertension Pulsus alternans may sometimes be heard especially if there is a *mitral* systolic murmur (Levine 1948)

Auricular fibrillation is found in about 7 5 per cent of unselected hypertensive patients (Rothstadt 1938) and may precipitate congestive heart failure At first and particularly if untreated it may be paroxysmal but as a rule it soon becomes persistent especially in elderly subjects Permanent *auricular fibrillation* under digitalis control is less troublesome than *paroxysmal fibrillation* and tends to protect the individual from paroxysmal cardiac dyspnoea and acute pulmonary oedema Other rhythm changes are relatively rare but *include auricular* flutter paroxysmal tachycardia and all degrees of heart block

Limitation of cardiac reserve is indicated by undue breathlessness on exertion and by poor responses to effort tolerance tests Left ventricular failure develops sooner *or later in the* majority of those who survive the other hazards of hypertension and may be recognised by a history of orthopnoea paroxysmal cardiac *dyspnoea* or pulmonary oedema and by finding a diminished vital capacity *maximum* breathing capacity and lung volume exaggeration of respiratory *intrathoracic* pressure swings prolongation of the crude pulmonary circulation time an increased pulmonary blood volume and *radiological* evidence of chronic interstitial

( pulmonary venous congestion ) as described on pages 273 to 279

Congestive heart failure with elevation of the venous pressure hepatic *distension and dependent œdema, follows left ventricular failure in practically* all cases that survive other risks Not infrequently, patients with hypertensive heart disease develop congestive heart failure without previous orthopnœa and paroxysmal cardiac dyspnœa There are two chief explanations for this behaviour (1) Left ventricular failure may result in a diminished cardiac output which reduces the renal blood flow and lead to retention of sodium and water the increased blood volume then raises the venous pressure so that the clinical features resemble those of failure of both ventricles although the right ventricle itself may not be overloaded (2) As in mitral stenosis passive pulmonary hypertension resulting from an elevated left atrial pressure may lead to active pulmonary vasoconstriction when the pulmonary vascular resistance exceeds 10 units right ventricular failure may be expected It should be explained perhaps that the pulmonary artery pressure is not ordinarily raised in systemic hypertension of any type or severity provided there is no left ventricular failure (Lenegre and Maurice 1947)

The suggestion that the right ventricle is partly obstructed by displacement of the interventricular septum (Bernheim 1910) lacks proof but the grounds on which the existence of Bernheim s syndrome is now be g rejected are premature and equally unconvincing It may clarify matters to restate the present position. The syndrome implies a severe left sided cardiopathy (such as hypertensive heart disease aortic valve disease mitral incompetence or cardiac infarction) with a form of left ventricular failure that presents clinically with a high venous pressure enlargement of the liver œdema and relatively little breathlessness but without orthopnœa, paroxysmal cardiac dyspnœa pulmonary œdema or radiological evidence of pulmonary venous congestion Bernheim s suggestion that a filling *defect of the right ventricle caused by undue bulging of the interventricular* septum might be responsible for the so called right ventricular failure was welcomed as a reasonable hypothesis to explain the physiological situation and after holding sway for forty years should not be abandoned *without adequate proof to the contrary*

Just as Eisenmenger s complex has had to be brought up to date by adding its most essential feature (a pulmonary vascular resistance at or above systemic level) so Bernheim s syndrome must be brought up to date by adding *absence of a high pulmonary vascular resistance a small right ventricle* and *considerable dilatation of the right atrium* As explained above the development of a high pulmonary vascular resistance (10 to 0 units) in cases of left ventricular failure can certainly prevent pulmonary congestive *manifestations just as it can in mitral stenosis* but in such instances the right ventricle is enlarged and the electrocardiogram may provide evidence of this in life This situation must be excluded before a diagnosis of Bernheim s syndrome is tenable The high resistance can be proved by

means of cardiac catheterisation in non ischæmic cases but the procedure is dangerous in patients with angina pectoris or previous cardiac infarction But if the pulmonary vascular resistance is not unduly high as in the case described by Selzer *et al* (1955) in which it was only 5 7 units what is protecting the lungs? Right ventricular failure should not occur from passive pulmonary hypertension (Wood 1954)

In some individuals with high left atrial pressures pulmonary congestive symptoms are curiously lacking despite the radiological demonstration of chronic interstitial œdema of the lungs but we are not concerned with these in the present discussion because one of the criteria upon which the modern diagnosis of Bernheim s syndrome rests is absence of this radiological sign

Selzer *et al* in their argument against the validity of the Bernheim concept compare the expected physiological situation with that in right sided constrictive pericarditis This is unsound partly because there is virtually no such thing as right sided constrictive pericarditis and partly because Bernheim s syndrome could not exist without left ventricular failure and a rise of left ventricular diastolic pressure A filling defect of the right ventricle implies impairment of a *diastolic* physiological function and the septum would not bulge unduly into the cavity of the right ventricle during diastole if the diastolic pres ure relationship between the two ventricles was reversed Pick s disease however considered conventionally serves very well to illustrate the Bernheim concept In this disease the left atrial pressure is usually of the order of 20 mm Hg which in uncomplicated mitral stenosis would certainly be sufficient to cause pulmonary congestive symptoms Why then are these symptoms usually absent? The answer of course is because the cardiac output cannot rise sufficiently to raise the left atrial pressure well above the osmotic pressure of the plasma This is just what might be expected if left ventricular failure were complicated by a filling defect of the right ventricle

One way of proving whether the right ventricle is overloaded or suffering from a filling defect would be to raise or lower the right atrial pressure by tipping or other means if the right ventricle is overloaded raising its filling pressure should reduce its output and therefore lower the pulmonary systolic pressure and the mean left atrial pressure if the right ventricle is suffering from a filling defect then raising the right atrial pressure should increase its output and therefore raise the pulmonary systolic pressure and mean left atrial pressure Or one might study the effect of inspiration and expiration upon the pulmonary component of the second heart sound with an overloaded right ventricle $P_2$ should not be delayed by inspiration whereas with a filling defect of the right ventricle it should be so delayed

The cardiac output is low in hypertensive congestive heart failure but may be near normal at rest in isolated left ventricular failure moreover paroxysmal cardiac dyspnœa may occur as the output rises (page 274)

The size of the heart in hypertension bears a close relationship to the

duration of heart failure it is largest in essential hypertension when failure has been protracted least enlarged in chronic nephritic hypertension when death is due to renal failure or in those who die from apoplexy or from other non cardiac causes (Harrison and Wood 1949) Again serial skiagrams may show little alteration in the manifest size of the heart for long period in essential hypertension yet gross enlargement may develop rapidly when failure occurs This is not only a matter of cardiac dilatation because heart weights show similar correlation Slight to moderate left ventricular hypertrophy probably results from hypertension alone according to its degree and duration but gross enlargement which usually involves the right ventricle as well as the left is always due to protracted failure

Moderate hypertrophy should be regarded as a compensatory change of structure which is beneficial it helps the heart to perform more work (Dieckhoff 1936)

*Electrocardiography* provides the most accurate means by which the degree of left ventricular enlargement and stress may be assessed Leads facing the surface of the left ventricle, such as V and $V_6$ show high voltage and slightly widened R waves with depressed R T segments and inverted T waves (fig 16 01) This fundamental pattern is reflected in right

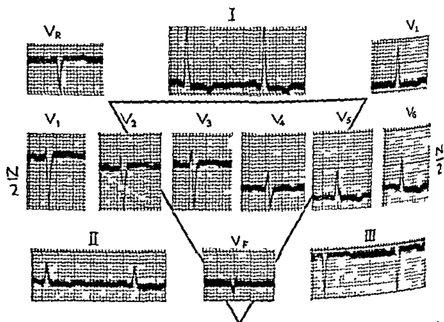



Fig 16 01—Electrocardiogram in a case of hypertensive heart disease (see text) The heart is electrically horizontal

ventricular surface leads such as V as small R waves followed by deep S waves the S T segment being elevated and the T wave invariably upright The heart is usually electrically horizontal left ventricular surface potentials being transmitted to the left arm right ventricular surface poten-

tials to the left leg Lead $V_L$ then resembles $V_5$ and $V_6$ lead $V_F$ resembles $V_1$ Standard limb leads therefore show left axis deviation, lead I looking like $V_L$ and lead III like $V_F$

*When the heart is rotated* clockwise on its longitudinal axis (viewed from below) the anterior part of the inter ventricular septum is displaced to the left and the transition zone shifts to the left of $V_4$ (fig 16 02) when the heart is rotated anti clockwise the transition zone moves to the right and QR complexes or dominant R waves with inverted T waves may be found as far across as $V_3$

When the heart is electrically vertical left ventricular surface potentials are transmitted to the left leg right ventricular surface potentials to the left

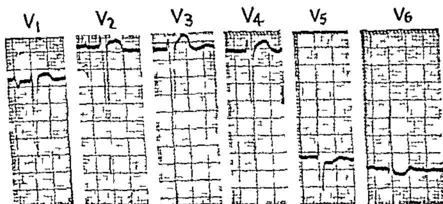



Fig 16 02—Electrocardiogram in a case of hypertensive heart disease with clockwise rotation about the longitudinal axis the transition zone is shifted to the left

arm Lead $V_F$ then shows the tall R wave and inverted T whilst lead $V_L$ has a prominent S wave Standard leads may then show right axis deviation with inversion of the T wave in leads 2 and 3

Concordant left ventricular preponderance in standard leads (fig 16 03) is due to a semi vertical electrical position of the heart Left ventricular surface potentials are transmitted to the left leg and standard leads show high voltage R waves and inversion of the T wave in all leads

The higher and wider the R wave in lead $V_5$–$V_6$ and the deeper the S wave in lead $V_1$ the bigger the left ventricle The pattern may be distinguished from left bundle branch block by the presence of Q in lead $V_6$ The cause of the R T segment depression and the T wave inversion is less well understood these changes may be associated with acute left ventricular stress without hypertrophy of the muscle although they usually result from both coronary disease is not responsible They are not altered by exercise or by transient reduction of the blood pressure to normal levels by means of hexamethonium or tetraethylammonium (Hayward 1948)

duration of heart failure it is largest in essential hypertension when failure has been protracted least enlarged in chronic nephritic hypertension when death is due to renal failure or in those who die from apoplexy or from other non cardiac causes (Harrison and Wood 1949) Again serial skiagrams may show little alteration in the manifest size of the heart for long periods in essential hypertension yet gross enlargement may develop rapidly when failure occurs This is not only a matter of cardiac dilatation because heart weights show similar correlation Slight to moderate left ventricular hypertrophy probably results from hypertension alone according to its degree and duration but gross enlargement which usually involves the right ventricle as well as the left is always due to protracted failure

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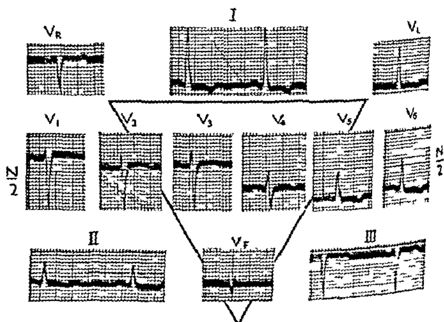



Fig 16 01—Electrocardiogram in a case of hypertensive heart failure (see text) The heart is electrically horizontal

ventricular surface leads such as $V_2$ as small R waves followed by deep S waves the S T segment being elevated and the T wave invariably upright The heart is usually *electrically horizontal* left ventricular surface potentials being transmitted to the left arm right ventricular surface po-



(a) Anterior view the apex of the left ventricle is buried in the diaphragm



(b) Angiocardiogram in the second oblique position

Fig 16 04—Hypertensive heart disease showing left ventricular enlargement

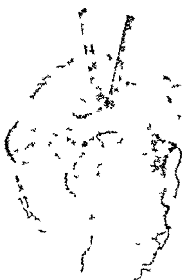


(a) Anterior view



(b) Left anterior oblique position with barium in the œsophagus

Fig 16 05—Skiagram of a case of hypertensive heart disease showing unfolding of the aorta






(a) (b)

ıg 16 06 Comparı ın of th ıronary stem in a n rm al (a) and a hyp rten ı e heart (b)
Th oronary el ha e be n inje ted with a radıo opaque gel ( ee text)




(a)



(b)

Fig 16 07—Coronary systems of two cases of hypertensi e heart di ea e ith angina pect
(a) Sho ing occlusi e coronary atheros cora (mixed ca e)
(b) Showing failure of the coronary essels to enlarge with the heart

*Angina pectoris* occurs in 5 to 10 per cent of cases and may be due to associated coronary atherosclerosis or to relative coronary insufficiency Conversely essential hypertension (past or present) has been found in 27 per cent of men and 71 per cent of women who present with coronary occlusion (Master 1953) Angina may be typical or it may tend to last longer than usual even up to an hour or so depending particularly upon transient rises of blood pressure such as occur, for example in paroxysmal hypertension strong emotion e g fear or anger and exposure to cold may provoke such an attack

It will be remembered that the coronary blood flow depends upon the mean blood pressure and upon the state of the coronary arteries During systole the large extra mural coronary vessels dilate forming a tense elastic reservoir the outflow being sealed by the intramural pressure The higher the systolic pressure the greater this elastic reservoir As the ventricles relax blood flows through the intra mural branches influenced not only by the aortic diastolic pressure but also by the elastic recoil of the superficial coronary arteries

Autopsy studies indicate that the coronary blood flow in essential hypertension is considerably increased In figs 16 06 the coronary systems of a normal and of a hypertensive heart are compared The vessels have been injected with a radio opaque substance at the calculated mean pressure and skiagrams have been taken at a fixed distance so that comparative measurements are valid The large and luxuriant coronary tree of the hypertensive case is typical of the series studied (Harrison and Wood 1949) It is probable that the coronary flow behaves like the blood flow through skeletal muscle and is usually increased in all forms of hypertension In cases of angina however skiagrams of the injected coronary vessels show either occlusive atherosclerosis (fig 16 07a) or a meagre coronary system which has failed to enlarge with the heart (fig 16 07b)

*Renal behaviour* varies greatly according to the type of hypertension In the essential variety renal failure is rare and when it does occur it is late usually in patients over 70 years of age Minor degrees of renal involvement however are common Traces of albumin, and hyaline casts are often found in the urine due to glomerular fault and diminished filtration may be revealed by inulin creatinine or urea clearance tests Tubular re absorption may be impaired resulting in polyuria and in diminished power of urinary concentration Nocturia may also be a feature

In malignant hypertension there is always a fast race between renal failure, cardiac failure and cerebral catastrophe The end is sometimes a combination of all three Nevertheless despite the early occurrence of renal failure it is rare for pronounced changes in renal function or for conspicuous urinary findings to precede the characteristic retinopathy (Wagener and Keith 1934) The converse is true of nephritic hypertension Nephrosclerosis in malignant hypertension differs from that found in

essential hypertension only in the presence of afferent glomerular arteriolar necrosis

In chronic nephritis there is usually considerable evidence of renal damage at a time when the heart is but little enlarged, and when the fundi are relatively normal Albumin, hyaline and granular casts and occasionally red cells, are found in the urine, inulin, creatinine and urea clearance are greatly diminished the blood urea may be raised and there is commonly polyuria nocturia, and failure of urinary concentration

*Cerebral manifestations* occur sooner or later in about one quarter of hypertensive cases *Cerebral hæmorrhage* is an ever present danger and may at any time cut short the life of the patient *Subarachnoid hæmorrhage* is by no means rare congenital deficiencies in the media or elastica of certain arteries, particularly those forming the circle of Willis with or without berry aneurysm giving way to the high pressure *Cerebral thrombosis* may also occur but depends more upon associated cerebral atherosclerosis

*Hypertensive encephalopathy* is characterised by attacks of severe headache vomiting coma or convulsions lasting for hours, with or without transient localising signs and is an important complication of malignant hypertension It is probably due to local or general cerebral ischæmia and œdema secondary to intense cerebral vascular spasm and increased capillary permeability (Scheinker 1948 Byrom, 1954) It should be understood that the normal cerebral blood flow in uncomplicated malignant hypertension implies intense cerebral vasoconstriction for if the cerebral vascular resistance remained normal the cerebral blood flow would be torrential with blood pressures in the region of 260/150 The rapid recovery that follows appropriate treatment (*vide infra*) and the ease with which appropriate prophylactic treatment prevents attacks deny both cerebral hæmorrhage and cerebral thrombosis although both may have to be excluded in the first instance

*Deterioration of higher cerebral function* has already been mentioned when severe it is usually due to associated atherosclerosis and ischæmia Occasionally however multiple pin point hæmorrhages scattered widely throughout the frontal lobes are found at autopsy and provide adequate explanation for dementia

*Hæmorrhages elsewhere* are not uncommon and include epistaxis hæmoptysis and hæmatemesis Whilst some local predisposing factor would seem probable, nothing significant is usually found Clinical diagnosis in such cases may be obscure at first, for hypertension may not be recognised owing to the fall of blood pressure which accompanies the hæmorrhage Moreover, when hæmodilution is slow, so that the hæmoglobin or hæmatocrit level is but little reduced the apparently normal blood pressure may lead to gross error of judgment concerning the size of the hæmorrhage Routine examination of the ocular fundi tends to prevent such mistakes

## DIFFERENTIAL DIAGNOSIS

If the blood pressure is found to be raised relative to standards already discussed a diagnosis of hypertension can be made and differential diagno is is concerned only with its cause

*Acute nephritis* should be obvious enough The distinction between *toxæmia of pregnancy* and essential hypertension in a pregnant woman is not always easy unless the previous or subsequent history is known Essential hypertension tends to be relieved during the second trimester for the peripheral resistance is lowered during a normal pregnancy Albuminuria sodium and water retention œdema elevation of the venous pressure breathlessness and a demonstrably rising blood pressure all indicate toxæmia of pregnancy It should be borne in mind however that the incidence of toxæmia in women with chronic essential hypertension is about seven times that in previously normal women (Browne 1947) so both may well be present *Coarctation of the aorta* is easily recognised if the femoral arteries are palpated as a routine *Cushing s syndrome* is suggested by obesity purple striæ high coloured moon facies hirsutism and amenorrhœa further studies are needed to elucidate the cause of the pituitary basophilism Functional overactivity of the adrenal cortex may lead to a rather similar syndrome (Shrœder *et al* 1949) A *hyperkinetic circulatory state* with high systolic pressure and less conspicuously raised diastolic pressure should be recognised by the tachycardia throbbing digital vessels bounding pulse and overacting heart Its cause may not be at all obvious and it should certainly not be attributed to an anxiety state or functional hyperadrenalism by a process of exclusion but only on positive grounds Hyperthyroidism arteriovenous fistula and Paget s disease of bone may be responsible for a hyperkinetic rise of blood pressure especially when there is coincidental atherosclerosis which increases the more proximal vascular resistance The degree of vasodilatation in hepatic failure and beri beri the reduced blood volume in severe chronic anæmia and the relatively slight increase of cardiac output in hypoxic cor pul monale do not encourage hyperkinetic systemic hypertension *Phæo chromocytoma* with a predominant outpouring of adrenaline rather than noradrenaline can cause a hyperkinetic circulatory state with chiefly systolic hypertension a test dose of rogitine is therefore advised in these difficult cases *Functional hyperadrenalism* should respond to rogitine equally well Personal experience suggests that there is also a non psychiatric form of hyperkinetic hypertension of as yet undetermined cause

*Paroxysmal hypertension* due to phæochromocytoma may be suggested by the history and confirmed by the rogitine or histamine type of test and by finding an excess of catechol amines in the plasm or urine (page 770)

The differential etiological diagnosis of persistent hypertension due to a high peripheral vascular resistance (after excluding phæochromocytoma and Cushing s syndrome) lies between chronic pyelonephritis other surgical kidneys chronic nephritis and essential hypertension

*Chronic pyelonephritis* may be suggested by the history, the absence of hypertension in the parents, pus cells and micro organisms in the urine early limitation of tubular concentrating power and the development of the malignant course in a relatively young subject (Brod 1955) Whether routine pyelography is justified when there is nothing to suggest chronic unilateral pyelonephritis is at least debatable Out of 2 055 routine pyelograms in subjects with persistent hypertension reported by Ratcliff *et al* (1947) less than 0 8 per cent were found to have an unsuspected unilateral renal lesion of a kind that led to nephrectomy and of this small number only about a third were so relieved of hypertension Since pyelography is not entirely without risk it is difficult to believe that its routine use is either wise or economically defensible for the sake of one patient out of 300 investigated Perhaps it should be restricted to those cases that might reasonably be suspected of having chronic pyelonephritis on the grounds given above

*Chronic nephritis* (chronic pyelonephritis and other surgical kidneys having been excluded) is a more likely etiological diagnosis than essential hypertension if impairment of renal function is far in advance of cardiac or cerebral disturbance or if renal failure occurs without heart failure in subjects under 60 years of age The differential etiological diagnosis between chronic nephritis and essential hypertension is no longer academic when hypertension is in the malignant phase

*Malignant hypertension* itself is diagnosed whenever there is papilloedema Etiologically almost any form of hypertension may take this course including acute nephritis visceral angiitis toxaemia of pregnancy phaeochromocytoma Cushing s syndrome pyelonephritis chronic nephritis and essential hypertension only coarctation of the aorta is exempt

## COURSE AND PROGNOSIS

The hypertension of *acute nephritis* is nearly always transient in those that recover After a latent interval which varies from a few weeks to very many years the blood pressure rises again in those that develop chronic nephritis The prognosis is then grave the mortality rate in men being six times that which would be expected in unaffected men of the same age group (Frant and Groen 1950)

Follow up studies on cases with *toxaemia of pregnancy* reveal that 30 per cent develop permanent essential hypertension (Light 1948) It is not clear however whether pre eclampsia is responsible for the subsequent hypertension or whether pregnancy merely precipitates the onset of essential hypertension The prognosis once persistent hypertension has developed appears to be the same as for essential hypertension

Perhaps the best follow up studies of persistent hypertension in the literature are those by Janeway (1913) Blackford Bowers and Baker (1930) and Bechgaard (1946) Janeway found that one half of 458 patients were

dead within five years and three quarters within ten years of the onset of symptoms Blackford Bowers and Baker reported a 56 per cent mortality (70 per cent of the men 9 per cent of the women) amongst 222 cases within five to eleven year Of Bechgaard s 1 000 patients 41 per cent of the men and 22 4 per cent of the women were dead within five to ten years The better outlook in women was emphasised in all three articles Bechgaard found the mortality rate of hypertensive men was 2 9 times and women 1 4 times that of the general population and was similar in all age groups (excluding renal cases)

Apart from sex the chief factors affecting prognosis include the type of hyperten ion the degree of retinopathy the height of the diastolic blood pressure and the state of the heart The natural outlook in malignant hypertension is uniformly bad few cases surviving more than one or two years and the average only 8 4 months after the diagnosis is fir t made (Schottstaedt and Sokolow 1953) Chronic nephritic hypertension also has a grave prognosis the mortality rate being about three times that of essential hypertension (Trant and Groen 1950) This is partly because renal hypertension is often a late manifestation of chronic kidney disease—hence the frequency of a normal sized heart in this group

Wagener and Keith (1939) correlated life expectancy with changes in the ocular fundi they followed the course of 200 patients for five to nine years The survival rate according to whether retinal changes were mild moderate severe or gross was 80 per cent 35 per cent 9 per cent and nil respectively When retinopathy was gross and included papillœdema, 80 per cent died within one year

Although the height of the systolic blood pressure is often said to matter little Sarre and Lindner (1948) found that in a series of 166 cases observed over a period of seven years 48 per cent of those with systolic pressures under 200 mm Hg survived compared with only 11 per cent of those with systolic pressures over 200 mm Hg It is generally agreed that high diastolic pressures are sinister in the series just quoted for example only 6 per cent of those with diastolic pressures above 140 mm Hg when first seen survived seven years

Cardiac behaviour in hypertension is determined by the amount of extra work involved and by the ability of the heart to cope with it it is chiefly influenced by the rapidity of hypertensive development by the size and strength of the left ventricle and by the efficiency of the coronary blood flow The best defence is put up by a placid patient of voluntary or enforced sedentary habits and occupation who has a naturally strong left ventricle with a good coronary blood flow when hypertension is neither too severe nor too sudden Under such circumstances the heart enlarges but little over the years failure is indefinitely deferred, and the patient remains free from cardiac symptoms The worst defence leading to rapid failure and perhaps to early death occurs in an excitable individual of active physical habits and strenuous occupation who tries to cope with a rapidly develop-

ing and extreme hypertension with an unprepared left ventricle indifferently nourished by a mean coronary system

Evidence of any cardiac abnormality e g diminished cardiac reserve angina pectoris enlargement or electrocardiographic changes at once doubles or trebles the mortality rate (Bechgaard 1946) Inversion of the T wave in left ventricular surface leads or their equivalent is particularly grave at least 60 per cent of such cases being dead in an average of eight months from the time of its discovery (Rykert and Hepburn 1935) Auricular fibrillation means death within two years in 80 per cent of cases (Rothstadt 1938)

Hypertensive heart failure is characteristically left ventricular at first and limits natural life expectancy to about eighteen months Systemic congestion follows sooner or later Several congestive attacks usually occur each responding less satisfactorily to treatment than its predecessor The patient finally sinks into a stuporose condition with chronic venous congestion hepatic engorgement and dependent dropsy the blood pressure falls Cheyne Stokes breathing develops and death comes slowly Heart disease is responsible for death in 33 per cent (Janeway 1913) to 55 per cent (Bell and Clawson 1928) of hypertensive cases stroke in 7 2 per cent (Paullin *et al* 1927) to 16 per cent (Bechgaard 1946) uraemia in 10 per cent (Bechgaard 1946)

The average life expectancy in uncomplicated benign hypertension of slight or moderate grade is about fifteen years (Fahr 1928) Obese subjects do as well or better than those with normal weight probably because their blood pressures are not as high as they seem when measured by means of standard cuffs Spontaneous recovery occurred in 5 4 per cent of Bechgaard s series (2 per cent of the women 13 per cent of the men) but in none of those seen by Blackford Bowers and Baker After five to ten years 58 per cent of Bechgaard s cases were free from symptoms or only slightly inconvenienced

Only about 0 2 per cent of cases of essential hypertension later become malignant but 8 per cent of cases of chronic pyelonephritic hypertension do so

## TREATMENT

It must be said at once that as yet there is no satisfactory treatment for essential or malignant hypertension When nephritic hypertension is due to a unilateral lesion such as chronic pyelonephritis nephrectomy has proved curative in 19 per cent of 242 cases (Smith 1948) but otherwise it can be but little influenced Moreover a causal relationship between a unilateral renal lesion and hypertension cannot be taken for granted and before advising nephrectomy it is as well to make sure that neither parent was hypertensive (Platt 1947) Normal renal function is also a necessary condition for successful nephrectomy for severe hypertension may have so damaged the vessels of the originally healthy kidney as to have made it

ischæmic and so to have established a vicious circle (Wilson and Byrom 1941) Good results from nephrectomy may be expected in 5 to 50 per cent of cases when the renal lesion is chronic uncomplicated unilateral pyelonephritis (Ratcliff *et al* 1947 Pickering and Heptinstall 1953)

The hypertension of Cushing s syndrome and that of phæochromocytoma both respond to removal of the offending tumour and that due to coarctation of the aorta to surgical repair

For essential hypertension there are six main lines of treatment (1) conservative (2) the low sodium or rice diet (3) a miscellaneous group of drugs acting on the central nervous system including rauwolfia veratrum hydrazinophthalazine and thiocyanate (4) adrenergic blocking agents such as hydergine (5) lumbo dorsal sympathectomy (6) ganglionic blocking agents such as hexamethonium and pentolinium

*Conservative* When the grade of hypertension is mild or moderate and when the prognosis is judged to be good on criteria previously outlined radical medical or surgical treatment is hardly justified but this does not mean that nothing else need be done Conservative treatment seeks to correct adverse factors and to prevent complications or deterioration

If circumstances permit it is a good plan to begin treatment by putting the patient to bed, and to keep him there until the blood pressure has reached a static level Symptoms usually disappear quickly and the patient gains confidence During this time renal function may be fully and conveniently investigated also the reaction of the blood pressure to bed rest gives useful diagnostic and prognostic information innocent labile types falling quickly to normal nephritic and malignant hypertension responding least

Patients should then be advised to live at a lower tempo they should learn to refuse extra commitments and to relinquish the least important or most irksome of those they already have they should keep Saturday and Sunday free for relaxation should have at least nine hours rest in bed every night and should insist on proper holidays each year preferably six weeks Long working hours heavy mental or physical stress and the general rush hurry and struggle of modern life must be avoided or reduced Occupation may require modification but it is rarely practicable to change it radically Sudden effort especially in the cold or after a heavy meal should be avoided straining at stool should be prevented by regular habits and if necessary by the use of liquid paraffin Alcohol in moderation is permitted, smoking should be strictly limited

Mental relaxation may be impossible without sedatives or psychiatric help Phenobarbitone ½ to 1 grain (32 to 64 mg) t d s may be prescribed at times of unavoidable anxiety alternated with potassium bromide 5 to 10 grains (0 32 to 0 65 G) t d s Psychiatric help is invaluable not necessarily from a psychiatrist but by any experienced physician with the requisite knowledge Many of the symptoms ascribed to hypertension are more often due to anxiety moreover hypertensive subjects usually have hyper-

*reactions to anxiety in the sense that their blood pressures rise unduly* (Hines 1940)

Symptoms attributed to hypertension at the menopause may respond to oral stilbœstrol 0 5 mg ethinylœstradiol 0 02 mg dienœstrol 1 mg or mepilin tab 1 *daily although the blood pressure does not fall* an associated anxiety state is also common at this time

Obese patients tend to do well on a weight reducing diet One day's bed rest with semi starvation per week diet then being limited to fresh fruit *fruit juice and water only may be most helpful or such a regime may be instituted at less frequent intervals when the patient feels the need of it*

With this simple regime 60 per cent of patients with essential hypertension remain free from symptoms until cerebral cardiac or renal com*plications arise*

Venesection has been advocated in the past and is still practised from time to time It is only justified in phlethoric cases associated with polycythæmia In essential hypertension its effect is fleeting the blood pressure *often regaining its previous level within twenty four hours* In malignant hypertension and in chronic nephritis venesection is contra indicated for some degree of anæmia is usually present in both conditions

Encephalopathy may be treated conservatively by means of rest and *vigorous dehydration Vestibular disturbances are relieved by* dramamine or avomine 25 mg three times daily (Goldman *et al* 1951) Heart failure responds to rest digitalis mercurial diuretics aminophylline and a low sodium diet Renal failure resists all therapy

*Low sodium diet* Although Allen and Sherrill in 1922 showed that a low salt diet was a potent means of lowering the blood pressure efficient dietetic treatment was not generally practised until re introduced by Kempner in 1944 Kempner's fruit rice diet consists essentially of fruit in any form fruit juices rice sugar and a little milk, it contains approximately 2 000 calories 20 G of protein 5 G of fat 200 mg of chloride and 150 mg of sodium (Kempner 1946) Lean meat fish and non leguminous vegetables without salt and fat may be added when the blood pressure has been satisfactorily controlled (Kempner 1948) Of 777 cases so treated the majority severe 70 per cent were unquestionably improved in an average time of three to four months (Kempner 1949) objective evidence included a fall in the sum of the systolic and diastolic blood pressure of at least 40 mm Hg disappearance of papillœdema and of retinal hæmorrhages and exudates restoration of an upright *T wave in standard lead I* (achieved in 50 per cent of cases in which it was previously inverted) and an appreciable reduction in the transverse diameter of the heart (51 per cent of 286 cases radiographed showed a reduction of about 6 per cent 37 per cent *a reduction averaging 14 per cent and* 6 6 per cent a reduction averaging 24 per cent)

The efficacy of a diet very low in sodium was confirmed in rats with experimental hypertension by Grollman and Harrison (1945) and in

human essential hypertension by Grollman (1945) It is now generally believed that its effect depends chiefly on its low sodium content (Pickering 1952)

Treatment of this kind is invaluable to relieve hypertensive crises including encephalopathy and severe retinopathy with impairment of vision it is also the best means of rapidly controlling left ventricular failure and congestive heart failure but its monotony precludes its routine use in uncomplicated essential hypertension for life expectancy may be ten years or more nor can it be used when there is gross impairment of renal function, for it may then precipitate uræmia For long term treatment however, a modified low sodium diet containing between 0 5 and 1 G. of sodium per day is advised With the help of lemon and herbs of all kinds such a diet (page 303) is well tolerated by the majority of patients whose personal experience has demonstrated its value and after six to twelve months some of them develop an active dislike towards salt A modified diet of this kind is insufficient by itself to control severe hypertension but it is a helpful adjunct to other forms of treatment and is imperative in cases with heart failure

*Rauwolfia serpentina*

Although a preparation of the root of rauwolfia serpentina has been used in India as a sedative since ancient times its value as a hypotensive agent has only recently been demonstrated (Vakil 1940 1949 1955 Bhatia 1942) The isolation of reserpine one of the most active of the rauwolfia alkaloids by Muller Schlittler and Bein (1952) was a notable advance

Reserpine 0 25 mg , is as active as 50 mg of the dried extract and more or less equivalent to 1 or 2 mg of preparations such as rauwiloid and hypertane which contain several of the other alkaloids of rauwolfia The initial dose of reserpine (serpasil) is 0 25 mg t d s , but it may be increased up to 0 5 mg t d s , or reduced to as low as 0 1 mg daily according to the response There can be no doubt that reserpine is a moderately potent hypotensive agent (Vakil 1953) It appears to act on the vasomotor centre itself in the hypothalamus A spate of literature has confirmed Vakil s results (e g Wilkins and Judson 1953)

*Side effects* include sinus bradycardia nasal congestion looseness of the bowels gain in weight coarse tremor or shakiness of the limbs vivid dreams drowsiness and mental depression

*Bradycardia* is beneficial in cases that present initially with hyperkinetic features and is never a disadvantage *Nasal congestion* may be very uncomfortable and should be treated with a suitable vasoconstrictor spray (such as privine) The *tendency to diarrhœa* helps to correct constipation in patients who are also treated with hexamethonium or pentolinium and is otherwise innocuous *Gain in weight* is due partly to the development of a hearty appetite and partly to retention of salt and water Both are serious

disadvantages the former particularly in cases with coincident coronary disease the latter when there is hypertensive heart failure (McGregor and Segal 1955) Dexamphetamine 5 mg one hour before breakfast and lunch may correct the increase of appetite and combat serpasil depression but *theoretically it would seem undesirable and is not* advised until trials have established its safety in these cases A low sodium diet given in conjunction with reserpine therapy prevents serious water retention *Shakiness of the limbs* is rare with doses not exceeding 0 25 mg t d s and usually disappears if the dose is reduced Coarse tremor seems to be Parkinsonian in type *Drowsiness* is beneficial at night but may interfere with efficiency by day the midday dose may then have to be withheld *Mental depression* may be intense and calls for immediate withdrawal of the drug for reducing the dose will not suffice This is fortunately unusual but must never be disregarded It has been suggested that depression is more common with reserpine than with preparations containing some of the other rauwolfia alkaloids but this has not yet been fully substantiated

Reserpine is not anti thyroid and does not increase the blood lipid *per se* As a rule coincident angina pectoris is not influenced by the treatment aggravation when it occurs may be attributed to gain in weight There is no evidence that the renal blood flow is reduced by rauwolfia alkaloids

*Veratrum*

*Veratrum viride* in the form of its powdered dry rhizome and roots was re introduced as a hypotensive agent for the clinical treatment of essential hypertension by Hite (1946) and Freis and Stanton (1948) A stable mixture of alkaloids biologically standardised was called veriloid (Stutzman *et al* 1949) and was found to be more easily managed clinically (Wilkins *et al* 1949) With initial doses of 2 mg t d s after meal increased gradually to 12 or 16 mg a day the blood pressure can be lowered in about two thirds of hypertensive cases (Kauntze and Trounce 1951) But side effects are the rule and include nausea and vomiting weakness and malaise and occasional collapse In the author s experience the patient s lack of well being while on veriloid precludes its long term use especially since it does not rank highly as a permanent hypotensive agent

*Veratrum album* has proved more valuable perhaps in that it has given us an active pure alkaloid protoveratrine (Krayer *et al* 1944 1946) which when given intravenously in doses of 0 1 to 0 15 mg may produce a profound fall of blood pressure in hypertensive patients (Meilman and Krayer 1950) thus it may be used intravenously with advantage in hypertensive crises For maintenance treatment protoveratrine is usually given by mouth *in doses of 0 4 to 2 0 mg* three times daily after meal start with the smallest dose and gradually increasing it until the desired therapeutic effect is achieved or until the limit of tolerance is reached Toxic symptoms, similar to those of veriloid are all too common and the

number of cases that can be successfully treated is less than 25 per cent (Doyle and Smirk 1953 Currens Myers and White 1953)

Veratrum like rauwolfia appears to act directly on the central nervous system (Stutzman Simon and Maison 1951)

*I Hydrazinophthalazine* is another hypotensive agent which may act centrally It has been given by mouth in doses of 50 to 150 mg four to six hourly but an appreciable fall in blood pressure is obtained in relatively few cases and side effects may be formidable—chiefly severe headache tachycardia and anxiety or depression (Shroeder 1952) moreover good results are transient (Johnson *et al* 1952) A short experience of this drug was sufficient for the author to abandon it permanently

*Thiocyanates* Thiocyanate was originally introduced as a hypotensive agent by Treupel and Edinger (1900) but gained no immediate favour in view of the difficulty experienced in avoiding serious toxic symptoms Considerable interest was taken in the drug however when Barker (1936) showed that the dose could be properly controlled if the thiocyanate blood level was estimated weekly The normal serum thiocyanate ranges between 0 and 2 77 mg per cent and is not altered in hypertension (Connell Wharton and Robinson 1946) Levels above 15 mg per cent are dangerous and those between 12 and 15 mg per cent are risky Toxic symptoms include weakness anorexia indigestion nausea vomiting limb pains impotence purpura dermatitis goitre thrombophlebitis mental lethargy and confusion In fatal cases dysarthria verbal aphasia convulsions hallucinations delirium and mania have usually preceded death by three to nineteen days (Del Solar *et al* 1945) Progressive anæmia and emaciation have been attributed to chronic poisoning after five to ten years continuous therapy (Wald Lindberg and Barker 1939)

The potassium salt was given by mouth in initial doses of 2 to 3 grains (0 13 to 0 2 G) three times daily after meals The serum thiocyanate was measured on the seventh day and then at weekly intervals subsequent dosage being regulated as follows

| *Thiocyanate level* | *Dosage recommended* |
|---|---|
| Under 5 mg per cent | 2 to 3 grains (0 13 to 0 2 G) t d s |
| 5 to 7 | 1 5 grains (0 1 G) t d s |
| 7 to 10 | 1 grain (64 mg) t d s |
| Over 10 | Stop drug for one week |

The lowest blood level compatible with a satisfactory hypotensive effect was maintained for three to six months Further courses were given as desired

The drug was said to be unsafe in patients over 60 years old who had had cerebral or other thrombosis or who had poor renal function but Watkinson and Evans (1947) observed no ill effect in fifteen patients

over 60 nor in sixteen cases of malignant or chronic nephritic hyper tension

Thiocyanates were particularly recommended for labile hypertensives who complained of headache and giddiness (Hines 1946) but they were also used for severe or gross cases unsuitable for lumbo dorsal sympathectomy and as an adjunct to surgical treatment Clinical benefit associated with a significant fall of blood pressure was claimed in about 60 per cent of cases (Watkinson and Evans 1947) This figure is not impressive when it is recollected that Bechgaard found that 58 per cent of 1,000 persistent hypertensives did well without treatment Carefully controlled observations such as those by Rusken and McKinley (1947) are more convincing and throw considerable doubt on the efficacy of thiocyanates It is well to remember that Pauli (1903), who is usually credited with introducing thiocyanate for the treatment of hypertension actually used the drug in the hope that it would prove superior to bromide in allaying anxiety symptoms and reported singular success in this respect Whether thiocyanate acts in this way or whether it has a more specific central hypotensive effect is still unknown but it is now considered too toxic for routine therapy and has been largely abandoned

*Adrenergic blocking agents*

Some confusion is attached to words like sympatholytic and adrenolytic, and it may help to define these terms A drug that blocks the response of effector cells to peripheral sympathetic nerve stimulation is said to be sympatholytic and since noradrenaline is the normal chemical mediator between the sympathetic nerve ending and the effector cell a sympatholytic substance is necessarily an adrenergic blocking agent A substance that blocks excitatory responses to *circulating* adrenaline and noradrenaline is said to be adrenolytic rather than sympatholytic but of course is also a adrenergic blocking agent The difference in actions between the two groups of drugs (although they always overlap to greater or less degree) is well exemplified in some of the diagnostic tests for phæochromocytoma For this purpose the best drugs are adrenolytic rather than sympatholytic and include benzodioxane and phentolamine (rogitine) dibenamine dibenzyline and ilidar have too powerful a sympatholytic effect to be reliable for this may lower the blood pressure in any kind of hypertension As therapeutic agents in essential hypertension it is the sympatholytic rather than the adrenolytic action that is needed and to this end hydergine is perhaps the best of the adrenergic blocking agents

Hydergine (1 ml ) contains 0 1 mg of each of the three dihydrogenated alkaloids of ergotoxine (dihydroergocornine dihydroergocrystine and dihydroergokryptine) Dihydroergocornine or hydergine may be given in doses of 0 05 to 0 1 mg intramuscularly or 0 1 to 0 5 mg orally three times daily (Freis *et al* 1949 Gibbs 1952) but seems to lose its effect after a few weeks (Moister Stanton and Freis, 1949)

Dibenamine priscoline and rogitine are of little value (Nickerson 1951)

*Lumbo dorsal sympathectomy* In recent years numerous attempts have been made to lower the blood pressure by surgical means The only operation that has proved eminently successful is nephrectomy in those relatively rare cases in which hypertension is due to unilateral renal disease such as chronic pyelonephritis Of other surgical measures the best known is lumbo dorsal sympathectomy as elaborated by Smithwick (1940) This consists of bilateral resection of the whole sympathetic chain from D8 to L2, including preganglionic fibres ganglia and splanchnic nerves The object is to release as much vasoconstrictor tone as possible to prevent renal cortical vasoconstriction to produce postural hypotension and of course to lower the basal blood pressure if possible With these aims there has been an increasing tendency to extend Smithwick s operation and a number of surgeons e g Grimson (1947) and Boyd (1948) favour either total or subtotal paravertebral sympathectomy splanchnicectomy and cœliac ganglionectomy

The results of these various procedures have been fair The operative mortality has averaged 3 9 per cent but about 25 per cent have died during the period of post operative observation (usually three to five years) There is no doubt that headache dizziness and other symptoms may be alleviated the blood pressure lowered the electrocardiogram improved the heart size reduced and retinopathy diminished by such means (Peet *et al* 1940) objective improvement of one kind or another has been demonstrable in about 66 per cent of cases (Smithwick 1944 1949)

In a series of 400 cases operated on for hypertension at the Massachusetts General Hospital (F M sex ratio 1 8 1) follow up studies showed that after one year postural hypotension had virtually disappeared after two years 38 per cent were improved and after five years 8 of 100 cases had normal blood pressures 13 had significantly reduced blood pressures 52 were much the same and 27 were dead (Evelyn *et al* 1949)

Of 143 cases of malignant hypertension treated by splanchnic resection by Peat and Isberg (1948) 21 6 per cent were still alive and free from papillœdema five years later the operative mortality was 10 per cent and no patient with moderate or marked impairment of renal function or with considerable cardiac enlargement did well

Although the long term results of surgical treatment were indifferent their historical value should not be underestimated for sympathectomy first proved that the blood pressure in essential hypertension could be permanently lowered occasionally even to normal and that lowering the blood pressure abolished the malignant reaction improved the patient s health and prolonged life thereby disproving the ill founded theoretical objection that to lower the blood pressure in essential hypertension without dealing with the disease itself (whatever that was supposed to mean) was unphysiological

Surgical sympathectomy thus opened the way to medical sympathectomy

and encouraged pharmacological research into blood pressure lowering drugs of all kinds

*Ganglionic blocking agents*

The demonstration by Burn and Dale in 1915 that tetraethylammonium ions inhibited transmission of all sympathetic and parasympathetic nerve impulses at the autonomic ganglia and the realisation how this action might be exploited (Acheson and Moe 1945) opened the way to medical sympathectomy Normally all autonomic impulses are chemically transmitted by means of acetylcholine which is liberated by the preganglionic nerve terminal and which then excites the ganglionic cells Ganglion blocking drugs prevent acetylcholine from acting on the ganglion cells (Paton 1951) In doses of 3 to 5 mg per kilo intravenously or about 10 mg per kilo intramuscularly tetraethylammonium releases vasoconstrictor tone both the blood pressure and venous pressure fall especially in the upright position the peripheral blood flow increases the skin temperature rises and the heart rate quickens These effects may be reversed immediately by peripherally acting adrenergic drugs such as noradrenaline Simultaneous parasympathetic block results in temporary paralysis of the gut and bladder dry mouth dry skin, dilatation of the pupils and loss of accommodation (Berry *et al* 1946 Lyons *et al* 1947) Peripherally acting cholinergic drugs such as acetylcholine mecholyl etc reverse these effects

*Pentamethonium iodide* (C5) and *hexamethonium iodide* (C6) or bromide introduced by Paton and Zaimis (1949) were found to be more powerful and more prolonged ganglionic blocking agents than T E A and were soon tried clinically for the relief of hypertension (Arnold and Rosenheim 1949 Burt and Graham 1950 Turner 1950) None of these early reports was enthusiastic fears that merely lowering the blood pressure was un physiological still lingered postural hypotension and fainting turns were regarded as serious drawbacks and the side effects from parasympathetic blockade were troublesome and occasionally dangerous In New Zealand however Smirk (1949) had perhaps a more enlightened view believing that the chief danger of hypertension was the high blood pressure itself however produced and that the object of treatment was to lower the blood pressure efficiently and keep it lowered postural hypotension properly harnessed became an asset rather than a liability and in conjunction with a low sodium diet methonium halides soon became the treatment of choice for the majority of cases of severe hypertension (Restall and Smirk 19 Smirk 1950 Smirk and Alstad 1951)

Hexamethonium bromide (vegolysen) may be given by subcutaneous injection in initial doses of 15 to 20 mg approximately three times daily the patient is preferably propped up in bed or may have the head of the bed raised on blocks so that orthostatic hypotension may be quickly recognised and corrected if too severe by lying the patient flat The blood

pressure should be recorded hourly both lying and standing Day by day the dose is increased by 10 to 20 mg according to the reaction and the rate at which tolerance develops the final dose may be 100 to 200 mg three times daily, but may have to be limited owing to side effects (*vide infra*) The objective is to maintain the blood pressure around the upper limit of normal when the patient stands up and to maintain it at this level for as long as possible during waking hours without causing serious side effects

Oral treatment requires doses of 250 to 750 mg thrice daily half to one hour before meals Unfortunately hexamethonium is very irregularly absorbed from the gut so that the correct dose is more difficult to arrive at and serious side effects may occur occasionally without warning

After a suitable single subcutaneous or intramuscular injection the clinical effect begins in 10 to 15 minutes and persists for several hours Within 24 hours 90 per cent of the drug is recoverable from the urine (Harrington 1953) Glomerular excretion is necessarily retarded in the presence of impaired renal function and if the blood urea is raised doses should be correspondingly small and infrequent if the drug is used at all

Undesirable side effects include constipation rarely intestinal paralysis retention of urine (particularly in patients with enlarged prostates) dry mouth, and disturbance of vision due to difficulty in accommodation The most dangerous of these is paralytic ileus which should be treated immediately with prostigmine 1 5 to 2 mg intravenously or intramuscularly and repeated two hourly if necessary no further doses of hexamethonium being given for at least 48 hours Laxatives are usually required as a routine to combat the tendency to constipation and patients should be advised to open their bowels before the morning dose of hexamethonium When serpasil is also used to help lower the blood pressure constipation is less troublesome Special reading glasses should be provided to compensate for the loss of accommodation

Weakness dizziness and pallor when standing still is due to orthostatic hypotension, and can be counteracted by walking about or lying down if dizziness is severe or if there is actual syncope the dose of hexamethonium should be reduced

Since bromine constitutes about 44 per cent by weight of hexamethonium bromide doses of 2 or more Grams per day orally are likely to result in symptoms of bromism sooner or later especially when patients are also on the low sodium diet These occur when the blood bromide exceeds 150 mg per cent and sometimes when it is only 75 to 100 mg per cent (Goodman and Gilman 1941) Hexamethonium iodide has a similar drawback in respect of iodism and the chloride is hygroscopic but the bitartrate 300 mg of which is equivalent to 250 mg of the bromide has none of these defects and is usually well tolerated Nevertheless with doses under 2 G daily hexamethonium bromide is preferred for its sedative action is an advantage

*Pentolinium tartrate* (M & B 2050 A or ansolysen) is about five times more potent and lasts one and a half times longer than hexamethonium (Wien and Mason 1953) moreover it is better absorbed from the gut more consistent results follow oral therapy (Maxwell and Campbell 1953) and hypertensive symptoms and complications (such as retinopathy) are controlled more swiftly than with hexamethonium (Smirk 1953)

If given by injection the initial dose should not exceed 4 mg, and increments should be small (2 mg) The initial oral dose is 20 to 40 mg three or four times daily half an hour before meals and this should not be increased by more than 20 mg per dose per day Management is otherwise the same as when using hexamethonium

*Combined methods of treatment*

The best all round results in the treatment of hypertension are undoubtedly obtained by combining rest the low sodium diet *rauwolfia alkaloids and pentolinium by mouth (Smirk et al 1954)* The treatment should be pressed home at the start until the blood pressure is normal or not above 160/90 in the standing position two hours after the last dose of pentolinium

The amount of each of the four therapeutic agents should then be adjusted to suit the patient until undesirable side effects are minimal and the regime tolerable and compatible with a reasonably active and enjoyable life This is usually possible while maintaining a good measure of control of the blood pressure

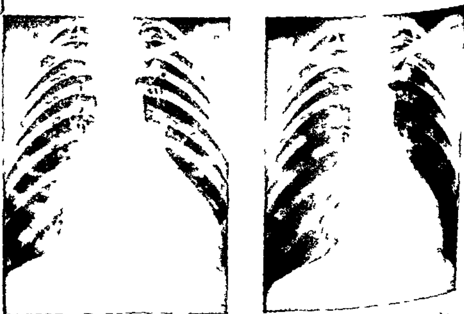


Fig 16 08—Skiagram (a) before and (b) after treatment of hypertensive heart failure by means of bed rest and a low sodium diet

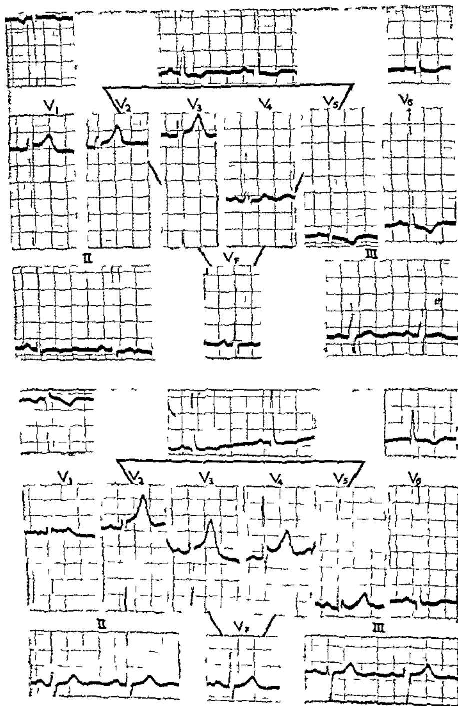



Fig 16 09—Electrocardiogram in a case of hypertensive heart disease (a) before and (b) after treatment with hexamethonium bromide and a low sodium diet Note the T wave changes in $V_4$ and V

Of the various manifestations of hypertension virtually all are relieved by combined therapy except nephrosclerosis. Headaches encephalopathy and retinopathy disappear rapidly in most instances Cerebral thrombosis is discouraged rather than encouraged by the fall in blood pressure The cerebral blood flow itself is not altered appreciably (Dewar *et al*, 1953) the cerebral vascular resistance falling more or less in proportion to the drop in blood pressure Left ventricular failure and congestive heart failure improve quickly and even some reserve can be built up in the more favourable cases (fig 16 08) Hypertensive T wave changes can be partly or wholly reversed (fig 16 09) in about half the cases (Doyle 1953) Angina pectoris is usually relieved but may be aggravated occasionally when the blood pressure falls steeply in cases with advanced coronary disease coronary thrombosis is no more common in treated than untreated cases (Doyle and Kilpatrick 1954) On effort the increased rise of blood pressure that ordinarily occurs in hypertensive subjects is suppressed (Fowler and Guz 1954)

Long term results of effectual medical treatment await the passage of the years but already it is obvious that the prognosis of malignant hypertension and hypertensive heart failure is at least twice as good as formerly Death from cerebral thrombosis, coronary thrombosis or renal failure rather than from heart failure is now the rule instead of the exception and patients live longer and in a better state of health in consequence

If treatment was undertaken much earlier at a time when it is often said to be worse than the disease the prospects might be brighter The most promising regime for early treatment is probably a combination of emotional relaxation and the rauwolfia alkaloids

While the treatment of transient hypertension cannot be considered here in detail it may be noted that toxemia of pregnancy responds very well to the low sodium diet veratrum (Assali *et al* 1950) progesterone 10 to 50 mg daily (Dalton 1954) and sympathectomy (Peat and Isberg 1949) it seems likely therefore that it should also respond to the combined treatment outlined above for essential hypertension

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that the percentage incidence of embolism is likely to appear higher in phlebothrombosis Fatal pulmonary embolism follows the injection treatment of varicose veins in 0 05 per cent of cases (Westerborn 1937) and the operative treatment in 0 4 per cent (Westerborn, 1937, McPheeters and Rice 1928)

Fractures particularly of the legs or pelvis may cause thrombo embolism on account of injury to veins immobilisation, and post traumatic acceleration of the clotting time, they may also give rise to fat embolism Malignant neoplasms especially carcinoma of the stomach may be responsible for thrombo embolism as a result of venous infiltration mechanical venous obstruction and shortening of the clotting time (owing to tissue necrosis) They may also give rise to malignant cellular emboli

The most common cause of phlebothrombosis is immobilisation in bed especially in obese subjects over 40 years of age Of 229 cases of fatal post operative pulmonary embolism Prettin (1936) found the average weight in women was 11 kg above normal and in men 4 2 kg In a series at the Mayo clinic, 93 per cent of fatal post operative pulmonary emboli occurred in patients over 40 years of age (Barnes 1937)

Congestive heart failure encourages phlebothrombosis because the circulation is slowed When the cardiac output remains elevated or is less reduced than usual as in failure from the hyperkinetic circulatory states thrombosis is rare Congestive failure due to mitral stenosis or to myocardial infarction is particularly dangerous Eppinger and Kennedy (1938) found that pulmonary embolism was the direct cause of death in 6 5 per cent of 200 fatal cases of coronary thrombosis and a contributory cause in 3 per cent of those with congestive failure The clotting time appears to shorten after myocardial infarction perhaps owing to the products of tissue necrosis The clotting time also appears to be shortened by digitalis (Massie *et al* 1944) and by the organic mercurial diuretics (Macht 1946) Clinically pulmonary embolism is recognised in about 10 per cent of cases with heart failure it is more frequent (20 per cent) in those with valvular disease than in those without (6 per cent) (Rissanen 1947)

Almost any major surgical procedure may result in thrombo-embolism, but abdominal and pelvic operations carry the highest embolic risk Responsible factors include post operative reduction of the clotting time (maximum at the tenth day) and immobilisation Child birth incurs a similar risk for similar reasons McCartney (1945) found that pulmonary embolism was directly responsible for 5 28 per cent of obstetrical fatalities and for 5 1 per cent of post operative deaths

## *HÆMODYNAMICS*

Experiments in which the pulmonary arteries have been occluded in varying degree by ligature or by artificial emboli have shown that it is necessary to obstruct about 60 to 85 per cent of their total cross section before the systemic blood pressure falls or before signs of right ventricular

failure can be detected and between 85 and 100 per cent before death ensues (Haggart and Walker 1923 Gibbon Hopkinson and Churchill 1932) It is thus possible to undertake unilateral pneumonectomy without embarrassing the circulation (Barnes, 1941) In accord with these facts the majority of pulmonary emboli cause no cardiac disturbance but when a large embolus lodges at the bifurcation of the main pulmonary artery or when multiple emboli block more than two thirds of the more distal trunks the circulation is impeded and the left ventricular output falls This is the condition known as massive pulmonary embolism and implies acute obstructive pulmonary hypertension Compensatory adjustments include vasoconstriction which combats the falling blood pressure elevation of the right ventricular pressure which helps to squeeze blood past the obstruction and elevation of the venous pressure which serves to encourage the right ventricle It is as yet uncertain whether that chamber usually becomes overloaded or not In cases which recover the embolus is gradually packed to the side of the vessel where it becomes organised and finally shrinks to a mere thread Infarction of the lung does not necessarily occur because sufficient blood may pass through to nourish the tissues

Subacute cases may occur in which repeated small emboli gradually block the pulmonary circulation over a period of weeks or months (Belt 1939) There is reason to believe that secondary pulmonary vasoconstriction may develop in some cases as a reaction to this subacute obstructive pulmonary hypertension and turn a potentially reversible situation into an irreversible state that closely resembles primary pulmonary hypertension (see page 833)

*Pulmonary infarction* When an embolus lodges distally in a relatively small arterial trunk there is no rise of pressure in the pulmonary artery blood is not squeezed past the obstruction and the block is complete infarction of that part of the lung supplied by the occluded vessel follows (unless the collateral circulation is sufficient to nourish the ischæmic area) Of course such an event is likely to complicate massive pulmonary embolism and does so in 62 per cent of cases (Belt 1934) but it is a complication and not an essential part of the picture Admittedly experimental pulmonary embolism does not cause infarction in animals unless the circulation is otherwise impaired (Karsner and Ash 1912) but no such condition appears to be necessary in clinical medicine Infarcts of the lung are hæmorrhagic because blood from the bronchial arteries exudes into the devitalised area If this second source of nutrition is adequate for the needs of the tissue infarction does not occur When the hæmorrhagic zone reaches the surface of the lung a sero fibrinous pleural reaction develops pain may be severe as in any other pleurisy effusion is common and is usually blood stained

Pulmonary infarcts are nearly always embolic in origin (Virchow 1856) very few are due to primary pulmonary thrombosis and they rarely com

plicate idiopathic pulmonary hypertension or Fallot's tetralogy, two diseases in which primary thrombosis is relatively common

## CLINICAL FEATURES

*Massive pulmonary embolism* In a typical dramatic attack the patient feels as if he had been struck in the centre of the chest and rapidly becomes faint, grey, cold, clammy and breathless Central sternal pain may be indistinguishable from that of acute myocardial infarction Consciousness may be lost Peripheral cyanosis is evident in the ears lips and nail beds but

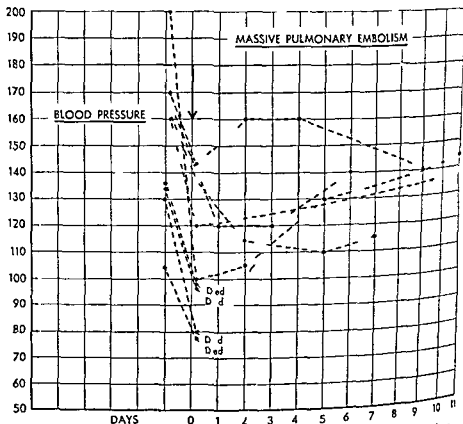



Fig 17 01—Behaviour of the blood pressure in 9 cases of massive pulmonary embolism. There is invariably a profound initial drop In the group shown those with relatively high blood pressures previously recovered whereas those with relatively low pressures previously died

elsewhere pallor is usually more noticeable Sweating is commonly profuse The pulse is thready and rapid, or may be imperceptible the blood pressure is low or immeasurable (fig 17 01) The jugular venous pressure is invariably raised (fig 17 02) and the liver may be palpable cardiac œdema is not seen in acute cases but may occur later in the subacute form Examination of the lungs may reveal nothing abnormal The heart sounds are usually soft, although the second sound at the base may be relatively accentuated

r widely split (if there is right bundle branch block) Clinical and direct visual evidence of dilatation of the pulmonary artery proximal to the embolus have been described by McGinn and White (1935) and by Churchill (1934) respectively The Graham Steele murmur of functional pulmonary incompetence has been heard (White and Brenner 1933) Occasionally a pericardial friction rub develops over the base of the distended pulmonary artery (White 1937)

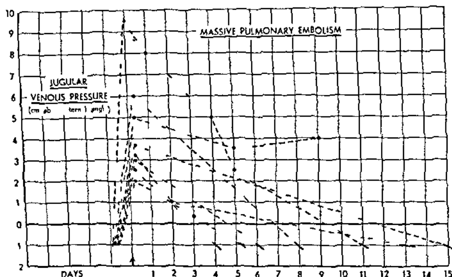



Fig 17 02—Behaviour of the venous pressure in 8 cases of massive pulmonary embolism There is initial elevation in all but it is rarely maintained for more than a few days

Rarely patients die abruptly at the onset presumably from reflex cardiac inhibition or ventricular fibrillation such deaths being preventable by atropine in animals and being independent of the size of the embolus (Scherf and Schonbrunner 1937) The great majority however survive the initial insult but about one third die subsequently from circulatory obstruction approximately 10 per cent within 10 minutes 30 per cent within an hour and 60 per cent in a matter of hours or days (de Takats and Fowler 1945) On the other hand about two thirds recover—within hours days or weeks Throughout this anxious period there is a 25 per cent risk of another and perhaps fatal embolus

Massive pulmonary embolism however is not always dramatic and mild cases are easily overlooked Passing tightness of the chest fleeting unexplained breathlessness transient faintness or a symptomless rise of systemic venous pressure may be the sole manifestation of an event that brought death very close

Subacute cases may pass gradually into congestive heart failure wi

a single incident suggesting embolism the clinical features of these rare cases resemble those of primary pulmonary hypertension

It should be noted that calling for the bed pan and *falling back dead* is not specially correlated with pulmonary embolism The phenomenon appears to be associated with impending death from ventricular fibrillation




Fig 17 03—*Electrocardiogram showing the characteristic appearances associated with massive pulmonary embolism (lead IV R—CR4 LP R—CR2 RP R=CR1)*

or asystole, and may occur as a tragic climax to many *forms* of heart disease including aortic stenosis and myocardial infarction The colonic disturbance may be a vagal manifestation Abrupt death from pulmonary embolism, preceded or not by a call to stool is rare as already mentioned

The diagnosis of acute right ventricular stress may be proved electrocardiographically (fig 17 03) Limb leads show sinus *tachycardia* a con

stant S wave in lead 1, a frequent Q wave in lead 3, inversion of $T_3$, flattening or slight inversion of T, and rather low voltage (Barnes, 1937). Occasionally P becomes tall and sharp (Wood, 1948). These appearances are not unlike those of posterior myocardial infarction, although an absent $S_1$, conspicuous Q and elevation of the R-T segment in lead 3 should be sufficient to distinguish the latter in standard leads. Again, $Q_3$ in cases of massive pulmonary embolism is caused by cardiac rotation, and is not seen

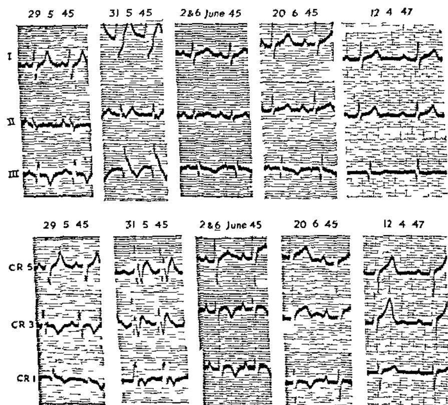



Fig. 17.04—Electrocardiogram showing transient right bundle branch block in a case of massive pulmonary embolism.

in lead $V_F$. In multiple chest leads appearances are equally characteristic (Wood, 1941): the T wave is nearly always inverted in leads $V_{1-3}$ over the right ventricle, sometimes in $V_4$ and occasionally even in V (fig. 17.03), and clockwise rotation or displacement of the interventricular septum to the left brings the RS pattern round as far as $V_5$ or even $V_6$. There are no pathological Q waves and the RS-T segment is not deviated from the base line, but in about 15 per cent of cases there is transient right bundle branch block (fig. 17.04). These changes are not immediate, but develop within a few hours, and are usually maximum within one to three days. Rec

should be made for the source As previously stated this is commonly phlebothrombosis in the legs It usually begins in the calf where there may be deep muscle tenderness, or pain on dorsiflexing the foot (Homans sign) If a pressure cuff is wrapped round the thigh and inflated to 40 mm Hg a characteristic pain develops in the calf when there is phlebothrombosis (Ortiz Ramirez and Serna Ramirez 1955) Superficial thrombosis in the long saphenous vein may be felt as a solid cord and is usually tender With thrombophlebitis the overlying skin is hot red indurated and painful Extension to the femoral vein causes a conspicuous rise of skin temperature in the affected limb a most useful sign of serious phlebothrombosis œdema also occurs in many cases but is less constant

## *PROGNOSIS*

It is not easy to assess the true mortality rate in thrombo embolism for many mild cases are overlooked, but in a consecutive series of twenty clinically recognised cases of massive pulmonary embolism seen by the author six died In necropsy material, about two thirds of all pulmonary emboli are major involving more than 50 per cent of the cross section of the pulmonary arteries (Belt 1939) but it is naturally the more severe ones that are seen at necropsy From evidence of this kind it is estimated that nearly two thirds of all cases of massive pulmonary embolism recover and that less than a third of clinical thrombo emboli are massive this gives a total mortality rate of about 10 per cent In those that recover there are ordinarily no sequelæ but there is an important though small group of cases in which subacute obstructive pulmonary hypertension leads to permanent and finally fatal chronic pulmonary hypertension

## *TREATMENT*

Prophylaxis is most important and should be directed towards accelerating the venous circulation in the legs and preventing the clotting process in bed ridden patients

Breathing exercises frequent changes of position, active movements of the legs for specified times every day prevention of dehydration and limitation of morphine are simple logical and effective measures Heart failure should be treated quickly and adequately Rest in bed should never be prolonged unnecessarily

*Heparin* is the quickest and safest anticoagulant but it is too expensive for routine prophylactic use It should certainly be employed however as soon as phlebothrombosis or thrombo embolism is recognised for 23 per cent are multiple (Nygaard *et al* 1940–41) and not more than a quarter of cases of massive pulmonary embolism are fatal at the first insult (de Takats and Fowler, 1945) Heparin may be given intravenously in doses of 50 mg (5 000 units) four to six hourly by continuous intravenous drip in doses of 150 to 300 mg daily (50 to 100 mg to a pint of normal saline) or intra

muscularly or subcutaneously combined with 2 ml of 2 per cent procaine in doses of 150 mg twice daily The last route is simple and effective Procaine prevents pain and local bruising is rarely serious The dose of heparin should be regulated so that the clotting time is maintained at about two to three times the normal (Murray and Best 1938) Pitkin s menstruum (gelatin 18 per cent dextrose 8 per cent glacial acetic acid 0 5 per cent distilled water to 100 per cent) as a vehicle for heparin to retard its absorption (Loewe *et al* 1946) is usually too painful for routine use

In the event of hæmorrhage the anticoagulant effects of 5 000 units (50 mg ) of heparin may be neutralised immediately by injecting 50 mg of protamine sulphate intravenously (Parkin and Kvale 1949)

Heparin is the sulphuric ester of a complex polysaccharide (Jorpes and Bergstrom 1937) and in view of the difficulty in preparing it from liver and therefore its expense strenuous efforts were made to find a sulphuric ester of some other polysaccharide that could be used as a substitute This search was rewarded by the discovery that several such esters had powerful anticoagulant properties including paritol (Sorenson and Wright 1950) treburon (Field *et al* 1953) and dextran sulphate (Ricketts *et al* 1953) The most promising and least toxic of these appears to be dextran sulphate Weight for weight paritol is one seventh as potent as heparin but its anticoagulant effect lasts two to three times longer treburon is one third as potent as heparin but lasts one and a half times longer dextran sulphate is put up in units that are equivalent to heparin but its effects last two to three times longer Paritol may cause swelling of the hands and feet and serious vasomotor collapse treburon has been reported to produce severe diarrhœa and late alopecia in some cases but has the advantage of being painless when injected intramuscularly dextran sulphate appears to be non toxic The heparin like action of dextran sulphate includes its ability to clear the turbidity of lipid laden plasma (Brown 1952) Its chief dis advantage is that it can only be given intravenously

*Dicoumarol* (3 3 Methylene bis 4 hydroxycoumarin) the cause of hæmorrhagic sweet clover disease of cattle (Link 1943) is a cheap and effective anticoagulant but its action is delayed for forty eight to seventy two hours and is cumulative so that it is difficult to control It acts indirectly by preventing the liver from manufacturing prothrombin Dicoumarol is given by mouth in single doses each day beginning with 300 mg the first day 200 mg the second and 100 mg the third sub sequent doses (usually 50 to 100 mg ) being adjusted according to the prothrombin time which should be kept as close as possible to two and a half times the prothrombin time in a normal control i e at a patient/control prothrombin ratio of 2 5 usually achieved with a maintenance dose of 50 to 100 mg daily In the past this ratio has been expressed reciprocally as an index i e $\frac{\text{control time}}{\text{patient s time}} \times 100$ or 40 per cent for a ratio of 2 5 T means that with a control time of 12 seconds, the patient s

time should be kept at 30 seconds The prothrombin time is inversely proportional to the prothrombin content of the plasma If the former is measured with increasing dilutions of plasma a graph may be constructed by plotting the prothrombin times against the respective plasma dilutions (or their reciprocals if the graph is to be a straight line instead of an impracticable rectangular hyperbola) If the patient s prothrombin time is read off on such a graph (constructed for normal plasma) it may be expressed in terms of prothrombin activity or content No practical advantage is gained by this manœuvre which has been the source of much confusion where there is no room for any misunderstanding whatsoever In fact a prothrombin ratio of 2 5 or index of 40 per cent is usually equivalent to an activity or content of 15 to 20 per cent It is solely to avoid any possibility of error that experienced physicians often prefer to chart the prothrombin time itself in seconds and to record the control time separately below

At first the prothrombin time should be measured daily, but as soon as the graph stabilises it may be estimated less frequently e g every second day then twice weekly, and finally once a week Frequent adjustments of the daily dose of dicoumarol are usually necessary at first but after a while it is easier to judge the right maintenance dose About 10 per cent of individuals are unduly sensitive to dicoumarol and an equal number unduly resistant the degree of sensitivity or resistance seems to be determined by heredity and changes little over the years

If the prothrombin ratio exceeds 3 microscopic hæmaturia may occur and if it exceeds 3 5 to 4 hæmorrhage may be serious or even fatal Hæmaturia malena and purpura occur in that order of frequency but a fatal hæmorrhage may be cerebral pericardial or retro peritoneal With proper laboratory control however, clinical hæmorrhage is rare (1 per cent) and a safe level of prothrombin activity can be restored immediately by blood transfusion or within a few hours by injecting 200 mg of vitamin $K_1$ intravenously (Douglas and Brown 1952) It has since been shown that 25 to 50 mg of vitamin $K_1$ orally is usually quite sufficient to restore normal prothrombin times and 15 to 25 mg to restore a satisfactory blood therapeutic level of prothrombin when it is desired to continue dicoumarol therapy (Toohey 1954) In the event of serious hæmorrhage it is hardly necessary to add that dicoumarol must be withheld at once whatever the prothrombin time for bleeds have been reported occasionally when the prothrombin activity has been well within the desired therapeutic range

When all goes well treatment should be continued for at least three weeks and preferably for six weeks in all cases of thrombo embolism and there should be no hesitation in continuing for three to six months in cases giving a history of recurrent thrombo embolic episodes

In view of the delayed effect of dicoumarol, heparin is usually given as well during the first forty eight to seventy two hours With this treatment the post operative mortality rate from massive pulmonary embolism in

cases specially selected as thrombo embolic risks has been reduced from perhaps 5 per cent to 0 1 to 1 0 per cent (Barker *et al* 1945 Wright 1946)

Many other coumarin derivatives have been shown to act like dicoumarol and have been used clinically as anticoagulants Some of them such as marcoumar [3 (1 phenyl propyl) 4 hydroxycoumarin] are even longer lasting and more cumulative than dicoumarol and therefore have little to recommend them for this property is a disadvantage Cyclocumarol (cumopyran) is in the same category Marcoumar, for example inhibits the manufacture of prothrombin for five days after a single dose Weight for weight it is very powerful the loading dose being 21 9 and 3 mg at daily intervals and the maintenance dose around 3 mg daily (Bourgain *et al*, 1954)

*Ethyl biscoumacetate* [bis 3 3 (4 oxycoumarinyl) ethyl acetate] introduced as tromexan and pelentan , is in a different class for its maximum effect occurs between eight and twenty four hours after a single dose and the prothrombin time returns to normal within the next eight to twenty four hours according to the size of the dose (Burt Wright and Kubik 1949) Being three to four times less active than dicoumarol the initial loading dose is high usually 900 600 and 300 mg at daily intervals, whilst the maintenance dose is commonly 300 to 600 mg daily it is also best given in divided doses two or three times daily (a tablet contains 300 mg ) Ethyl biscoumacetate however is expensive and has been largely replaced by dindevan

*Sinthrone*, which is 3 [α (4′ nitrophenyl)β acetyl ethyl] 4 oxycoumarin is probably the best of the coumarin derivatives for clinical purposes in that a therapeutic level of reduced prothrombin activity can be achieved easily in twenty four to forty-eight hours and maintained steadily on a small daily maintenance dose whilst there is little cumulative effect The loading do e is 24 mg the first day 16 mg the second and 4 to 8 mg thereafter according to the prothrombin ratio (Moeschlin and Schorno 1955) Sinthrome is put up in 4 mg tablets

*Phenylindanedione* (2 phenylindane 1 3 dione) or dindevan appears to approach the ideal therapeutic drug of its class and is the most active prothrombopenic agent of the indanedione derivatives (Soulier and Gueguen 1947 1948) moreover it is much cheaper than tromexan Its effect on the prothrombin time is maximum between twenty four and thirty six hours after a single dose and it has virtually no effect after forty eight hours (Toohey 1953) Given in divided doses twice daily it therefore keeps the prothrombin level steadier than tromexan on the other hand its relatively short period of activity, and the absence of a cumulative effect make it much safer and easier to manage than dicoumarol Phenindione as it is now being called is non toxic but dermatitis apparently due to the development of hypersensitivity to the drug developed in two of my own cases The loading dose is 150 to 200 mg on the first day 100 mg on the second and 50 mg on the morning of

third for maintenance 50 to 150 mg daily is usual Tablets contain 50 mg but are scored so that 25 mg doses may be given

Hæmorrhages are rare with the shorter acting prothrombin depressors and relatively small doses of vitamin $K_1$ (10 to 15 mg orally or 5 mg intravenously) are usually sufficient to restore safe prothrombin levels within twenty four hours if an overdose has been given (Toohey 1954 Dawson 1955) Nevertheless it must never be forgotten that all anticoagulants are potentially dangerous and should not be given lightly or without proper laboratory facilities nor should they be given to any patient with an active peptic ulcer or with a recent history of spontaneous hæmorrhage from any source They should be withheld temporarily in the event of any surgical operation dental extraction or infective hepatitis

*Bilateral ligation of the femoral or common iliac veins or ligation of the inferior vena cava* has been received with less enthusiasm but it may be a life saving procedure when anti coagulants are contraindicated Subsequent œdema when present, usually passes off within three months and little detrimental clinical or physiological effects can be detected as a rule (Burch and Ray 1947) Recurrent superficial thrombophlebitis however may prove troublesome

*Treatment of acute obstructive pulmonary hypertension*

Relatively mild cases recover spontaneously and require no special treatment The majority of those clinically recognised however a seriously ill and require urgent attention The objective is very simple it is to keep the patient alive long enough for the clot to retract and so relieve the obstruction at the same time further emboli must be prevented at all costs To this end the following procedures should be carried out immediately

1 The patient should be nursed flat in order to encourage the cerebral circulation Warmth should not be applied to the body and vasodilating agents should not be given with the idea of dilating the pulmonary artery for these merely serve to lower the blood pressure which is already critically reduced and can have no influence on the large pulmonary vessels

2 Oxygen should be given through a light plastic mask or the patient may be nursed in an oxygen tent so that the litre or two of blood that is passing through the lungs may be supersaturated with oxygen

3 The basal vasomotor and respiratory centres must be supported for their collapse means instant death For this purpose nikethamide (coramine) has no equal and it should be given in doses of at least 0 5 to 1 G (2 to 4 ml of the standard 25 per cent solution) intravenously as often as required (even every five minutes in desperate situations) and if there is no response to 1 G the dose should be doubled Nikethamide is rapidly inactivated in the blood stream and there is therefore no danger of a cumulative effect An overdose however may give rise to convul io

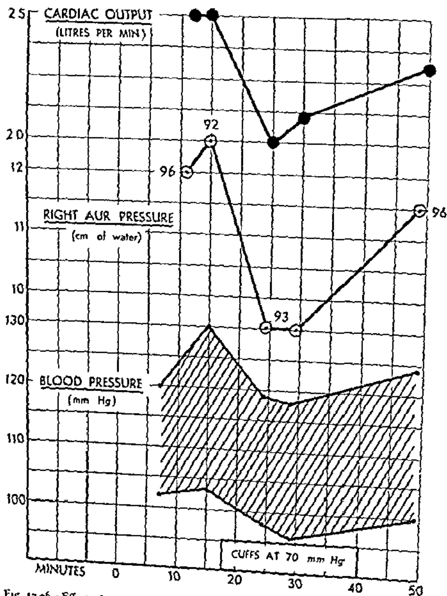



Fig 17 06—Effect of a venous pressure lowering agent (cuffs on the thighs) on the blood pressure and cardiac output of a case of massi e pulmonary embolism

Morphine is contra indicated in view of its depressing effect on respiration, and pethidine is also better withheld in view of its vasodilating action at least until the situation is under control

4 The blood pressure must be maintained by means of noradrenaline aramine or mephentermine (wyamine), as described on page 749

5 Heparin 10 000 to 15 000 units should be given intravenously at once, and repeated in doses of 5 000 to 10 000 units four to six hourly during the first forty eight hours As soon as the patient is able to swallow 200 mg of phenylindanedione should be given followed by 100 mg the following day subsequent doses being regulated according to the prothrombin ratio Anticoagulant treatment must be maintained at a high therapeutic level (ratio nearer 3 than 2) for at least three weeks, or until the danger of recurrent embolism is passed

6 Ouabain or digoxin 1 mg may be given intravenously if the venous pressure is more than 5 cm above the sternal angle at 30 degrees on the chance that the right ventricle is overloaded and 0 5 mg doses may be repeated twice at six hourly intervals In a typical case of the author's however lowering the venous pressure resulted in a fall of cardiac output and blood pressure (fig 17 06) suggesting that the right ventricle was not overloaded

The Trendelenburg operation (Trendelenburg 1908)—exposure of the pulmonary artery and removal of the clot—is only possible if a well trained and thoroughly prepared surgical team is available and is only practised when the situation is desperate the operative mortality is over 90 per cent (Nygaard 1938) and spontaneous recovery is the rule rather than the exception The first successful embolectomy in Great Britain was reported by Ivor Lewis in 1939

*Treatment of pulmonary infarction* No specific treatment is required for pulmonary infarction itself but secondary infection or septic embolism calls for penicillin or other suitable antibiotic, morphine may be necessary if there is severe pleural pain and hæmorrhagic pleural effusion may need aspirating if extensive Infarction does not contraindicate anticoagulants

## PARADOXICAL EMBOLISM

Valvular patency of the foramen ovale is present in about a third of all individuals but the opening remains closed because the pressure in the left atrium is higher than that in the right When the right ventricle fails however the atrial pressures may be reversed the valve then opens and blood is shunted from right to left This event is improbable in heart failure secondary to mitral stenosis for the left atrial pressure remains too high Ideal conditions are presented by acute right ventricular failure due to massive pulmonary embolism for not only is the right atrial pressure then raised but the left is lowered as in pulmonary stenosis, and emboli are

already forthcoming Having passed through the foramen ovale the embolus is carried into the systemic circulation and may lodge in any cerebral visceral or peripheral artery

## AIR EMBOLISM

Small quantities of air may be injected into the systemic venous system of healthy subjects with little risk indeed about 15 ml per kg body weight are required to kill a dog even when injected rapidly (Wolffe and Robertson 1935) Fatalities have occurred however when air has been accidentally introduced into a vein during an operation intravenous infusion therapeutic or diagnostic procedure The clinical features are those of massive pulmonary embolism but in addition a loud churning sound or millwheel murmur may be heard over the right ventricle and pulmonary artery Death appears to result from circulatory obstruction due to air lock in the outflow tract of the right ventricle Treatment consists of turning the patient into the left lateral position in the hope of displacing the air into the right atrium (Oppenheimer Durant and Lynch 1953) A similar manœuvre has proved life saving in dogs but has not yet been tried in man

## FAT EMBOLISM

Globules of fat may penetrate the systemic venous circulation following fractures usually of the femur and accidents have occasionally occurred during therapeutic or diagnostic procedures involving the use of oil Fat embolism has several characteristics which help to distinguish it from other forms First it happens within a few hours of the accident perhaps while manipulating the injured limb under anæsthesia or when moving the patient to the X ray department Second signs of multiple systemic embolism usually complicate the picture owing to the passage of fat globules through the pulmonary capillaries Thus there may be severe headache drowsiness or loss of consciousness usually without localising signs multiple petechial spots may appear in the skin red cells albumin and droplets of oil may be found in the urine Third breathlessness and cyanosis are associated with the development of fine crepitations over all areas of the lungs and skiagrams show an abundance of cotton wool shadows in all zones The mortality rate is similar to that of other forms of massive pulmonary embolism but those who survive recover remarkably quickly – often within forty eight hours

## EMBOLISM DUE TO FOREIGN BODY

Metallic fragments from gun shot wounds and even bullets may enter the circulation in rare instances Such an event should be considered if a skiagram shows an intra thoracic foreign body when there is no wound of the chest or adjacent structures An intravascular metallic foreign body may remain mobile for several days and may move against the bloodstream if so directed by the force of gravity Surgical attempts to remove a

missile may be foiled by such behaviour An excellent example was described by Bauer (1943)

## MALIGNANT EMBOLI

Cancer cells may infiltrate the systemic venous system and be swept into the lungs in the form of cellular emboli Subacute pulmonary hypertension develops if more than two thirds of the vessels are blocked the clinical features resembling those of massive pulmonary embolism but with an insidious onset and progressive course The diagnosis may be suggested by the skiagram which may show minute miliary lesions (fig 17 07) Cases so far reported have been due either to carcinoma of the stomach (Brill and Robertson 1937) or breast (Mason 1940) or to chorionepithelioma (fig 17 08)



Fig 17 07—Skiagram showing miliary embolic carcinomatosis of the lungs



Fig 17 08—Radiological appearances of the lungs showing embolic secondaries due to chorionepithelioma

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Subacute pulmonary hypertension may also be due to multiple pulmonary thromboses secondary to perivascular lymphatic carcinomatous infiltration (Brill and Robertson 1937) As a rule however, these cases present with subacute hypoxic cor pulmonale (q v )

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Fig 17 07—Skiagram showing miliary embolic carcinomatosis of the lungs



Fig 17 08—Radiological appearances of the lungs showing embolic secondaries due to chorionepithelioma

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tension develops if more than two thirds of the vessels are blocked the clinical features resembling those of massive pulmonary embolism but with an insidious onset and progressive course The diagnosis may be suggested by the skiagram which may show minute miliary lesions (fig 17 07) Cases so far reported have been due either to carcinoma of the stomach (Brill and Robertson 1937) or breast (Mason 1940) or to chorionepithelioma (fig 17 08)

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## CHAPTER XVIII

# PULMONARY HYPERTENSION

*Normal pulmonary blood pressure*

The average normal pulmonary blood pressure is 16/7 mm Hg (mean 11 mm Hg) with reference to the sternal angle This figure is based on fifty normal controls investigated by the author for one reason or another over the past eight years The cardiac output at the time ranged between 5 8 and 12 8 litres per minute (average 8 6) As repeatedly pointed out conditions are not basal during cardiac catheterisation The normal mean left atrial pressure averages 2 to 3 mm Hg above the sternal angle so that the normal pulmonary artery-left atrial pressure gradient is 8 to 9 mm Hg and the pulmonary vascular resistance (page 177 is therefore $\frac{8 \text{ to } 9}{8\ 6}$ or around unity (80 dynes sec/cm [5]) Conventional figures are 10 mm Hg for the gradient 5 litres per minute for the cardiac output and 2 units for the resistance

*Definition and classification of pulmonary hypertension*

Pulmonary hypertension literally implies a pulmonary blood pressure above 30/15 mm Hg which is the upper limit of the normal range Physiologically there are four entirely different mechanisms that may produce pulmonary hypertension namely appreciable elevation of the left atrial pressure obstruction or obliteration of more than two thirds of the total cross section of the pulmonary vascular bed at any level a sufficiently increased pulmonary blood flow and active pulmonary vasoconstriction each of these mechanisms causes its own particular variety of pulmonary hypertension which may be labelled respectively passive obstructive or obliterative hyperkinetic and vasoconstrictive There is no doubt that any form of pulmonary hypertension if sufficiently severe and prolonged finally produces sclerotic changes in the pulmonary arteries with or without local thromboses which may add an obliterative or obstructive element to the picture and there is good reason to suspect that any form of pronounced pulmonary hypertension may also excite a vasoconstrictive reaction and so turn passive obstructive or hyperkinetic pulmonary hypertension into the more serious vasoconstrictive type Such a reaction would close a vicious circle and so transform a relatively innocent pulmonary hypertension into a more or less malignant form The parallel between this hypothesis and current theory in respect of systemic hypertension will not pass unnoticed

## PASSIVE PULMONARY HYPERTENSION

Mean left atrial pressures of 20 to 30 mm Hg at rest and 40 to 50 mm Hg on effort are common in mitral stenosis In such cases the mean pulmonary artery pressure must be at least 10 mm Hg higher if the normal pressure gradient is to be preserved A similar situation arises in mitral incompetence and left ventricular failure This may be called passive pulmonary hypertension because it represents no more than transmitted pulmonary venous hypertension Left atrial pressures of 15 to 20 mm Hg and therefore mean pulmonary artery pressures of 25 to 30 mm Hg are usual in chronic constrictive pericarditis and in cases of congestive heart failure due to any generalised cardiopathy such as isolated myocarditis but they do not rise on effort because the right ventricle is incapable of increasing its stroke output Passive pulmonary hypertension in these cases is therefore trivial

Reactive pulmonary vasoconstriction raised the pulmonary vascular resistance to between 6 and 10 units in 16 per cent of 275 critical cases of mitral stenosis studied by the author and to over 10 units (average 17) in 12 per cent By critical is meant sufficient stenosis (orifice around 1 × 0 5 cm) to raise the left atrial pressure 20 mm Hg or more when the cardiac output is 4 to 5 litres per minute and the heart rate normal i e sufficient to cause a mean pulmonary artery pressure over 30 mm Hg at rest Reactive pulmonary vasoconstriction does not seem to occur in response to less passive pulmonary hypertension than this Whether it is persistent pulmonary hypertension of the order of 50/25 mm Hg or repetitive pulmonary hypertension of a much higher degree that is responsible for the vasoconstrictive reaction is unknown indeed, there is no direct proof that it is the pulmonary hypertension that is causing the vasoconstrictive reaction at all Certainly the historical and objective lack of chronic interstitial œdema of the lungs in cases with an extreme resistance exonerate that factor as a possible etiological agent

The incidence of active pulmonary vasoconstriction in mitral incompetence appears to be lower Of 58 cases severe enough to have warranted mitral valve repair had such an operation been available only 14 per cent had an appreciably increased pulmonary vascular resistance (9 per cent between 6 and 10 units and 5 per cent in the extreme range over 10 units) The lower *mean* left atrial pressure and lower mean level of passive pulmonary hypertension may explain this lower incidence of the vasoconstrictive response Alternatively the factor that seems to limit right ventricular filling in severe mitral incompetence (Bernheim effect or increased pericardial tension?) may prevent surges of right ventricular output and undue rises of pressure on effort Certainly an increased pulmonary venous or arterial pulse pressure which is characteristic of mitral incompetence cannot be responsible for reactive vasoconstriction or the latter would be more common in mitral incompetence than

No figures are available for the frequency of active pulmonary hypertension secondary to the passive pulmonary hypertension of left ventricular failure. It was observed on page 774, however, that many cases that present clinically with the Bernheim syndrome prove to be examples of right ventricular failure secondary to reactive pulmonary vasoconstriction.

No instance of extreme pulmonary vasoconstriction has yet been recorded secondary to the relatively mild passive pulmonary hypertension of Pick's disease and generalised cardiopathies. This again suggests that a critical level of pulmonary hypertension must be reached before significant reactive vasoconstriction occurs.

The clinical details of passive pulmonary hypertension and its vasoconstrictive response (Wood, 1954) have already been discussed in relation to mitral valve disease on page 540 and to left ventricular failure on page 774.

## HYPERKINETIC PULMONARY HYPERTENSION

As the blood flow through the lungs increases, the vessels dilate to accommodate the extra volume and temporarily closed vessels probably open up, so that the resistance falls; there is thus little or no rise of pressure at first (Hickam and Cargill, 1947; Riley *et al.*, 1948); but as the flow approaches three times the normal (15 litres per minute in an adult of average height and weight) a state of maximum vasodilatation is reached and no further drop in resistance is possible; thereafter the pulmonary blood pressure rises in proportion to the flow (Cournand, 1950). In other cases the pulmonary vascular resistance does not alter much with effort, the pulmonary blood pressure tending to rise with quite small changes of output (Dexter *et al.*, 1951; Donald *et al.*, 1955). In disease both types of response are seen. For example, pulmonary blood flows of 10 to 15 litres per minute, reduced resistance and no appreciable rise of pulmonary blood pressure are characteristic of many cases of atrial septal defect; in the majority of cases of patent ductus or ventricular septal defect, on the other hand, flows of this order are usually associated with some rise of pressure, the resistance being normal (or even slightly raised) rather than unduly low. With flows of 20 to 30 litres per minute the pulmonary blood pressure may approach and even reach systemic level. Hyperkinetic pulmonary hypertension then may be defined as a raised pulmonary blood pressure associated with an increased flow and normal resistance.

In the generalised hyperkinetic circulatory states, such as thyrotoxicosis, beri-beri, Paget's disease of bone, anæmia, cor pulmonale, hepatic failure, pregnancy, and phæochromocytoma of the adrenaline (rather than nor-adrenaline) type, the frequency of hyperkinetic pulmonary hypertension is not yet known, but there can be little doubt that it may occur, especially perhaps in beri-beri. The increased pulmonary blood flow in cor pulmonale is particularly important because it may be associated with some degree

of obliterative pulmonary hypertension and the combination may be responsible for very high pulmonary blood pressures

Of the congenital shunts there are at least five acyanotic and five cyanotic forms that may result in hyperkinetic pulmonary hypertension

| *Acyanotic* | *Cyanotic* |
|---|---|
| Partial anomalous pulmonary venous drainage | Total anomalous pulmonary venous drainage |
| Atrial septal defect | Single atrium |
| Ventricular septal defect | Single ventricle |
| Patent ductus arteriosus | Persistent truncus |
| Aorto pulmonary septal defect | Transposition of the great vessels |

These have all been discussed in detail in the chapter on congenital heart disease

*Appreciable reactive pulmonary vasoconstriction* occurred in one quarter of a consecutive series of 100 critical cases of atrial septal defect and two thirds of 100 critical cases of patent ductus or ventricular septal defect studied by the author By critical is meant a defect of sufficient size to cause a pulmonary blood flow of at least three times the systemic flow in the presence of a normal pulmonary vascular resistance Clinically this means that the case would be regarded as severe or gross rather than mild or moderate in degree In the 93 cases that had developed the vasoconstrictive response the pulmonary vascular resistance lay between 6 and 10 units in 29 and between 10 and 30 units (average 17) in 64 This suggests that if the reaction occurs at all it is likely to become extreme The presence or absence of the vasoconstrictive response was obviously determined at birth in the great majority if not in all cases and the idea that pulmonary hypertension due to a high pulmonary vascular resistance develops slowly over the years is totally unsupported by all available data Obstructive pulmonary hypertension due to embolism or thrombosis may occur suddenly in the later stages of these diseases but that is another matter altogether The evidence suggests that in one group of individuals hyperkinetic pulmonary hypertension at once causes persistent pulmonary vasoconstriction whereas in another group of individuals it does not The secret of this difference in behaviour has not yet been discovered nor is it yet understood why cases of atrial septal defect are less likely to develop the reaction than cases of patent ductus and ventricular septal defect of comparable severity

The clinical features of hyperkinetic pulmonary hypertension and the effect of the vasoconstrictive reaction on the physiology of the circulation in all these congenital anomalies have already been described in Chapter VIII and cannot be further considered here

## OBSTRUCTIVE OR OBLITERATIVE PULMONARY HYPERTENSION

The word obstructive is best applied to massive pulmonary embolism or thrombosis and to subacute miliary thrombo embolism or widespread peripheral pulmonary thromboses pneumonectomy also provides an example of artificial obstruction of half the total cross section of the pulmonary vascular tree Carcinomatous embolism and diffuse infiltrative lymphatic carcinomatosis behave rather differently and will be described as a form of subacute cor pulmonale in Chapter XIV although secondary widespread thromboses may also cause obstructive pulmonary hypertension The term obliterative more accurately describes the situation in respect of the capillaries in emphysema and the small arteries and arterioles when they are partially or wholly blocked by gross endocardial thickening as an anatomical reaction to severe and prolonged pulmonary hypertension of any kind, secondary to subacute thrombo embolism or as a result of certain forms of arteritis including periarteritis nodosa disseminated lupus and schistosomiasis Secondary thrombosis is common in these partially occluded vessels so that obstructive and obliterative types may overlap

*Massive pulmonary embolism* was considered fully in the last chapter

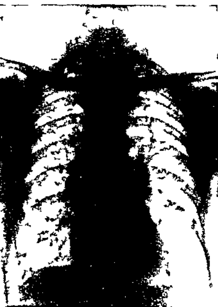
*Massive pulmonary thrombosis* is relatively rare but may complicate any form of long standing pulmonary hypertension that has developed extensive pulmonary atherosclerosis Its pathogenesis is comparable to thrombosis at the distal end of the descending aorta in elderly men with gross aortic atherosclerosis

The degree of obstructive pulmonary hypertension produced obviously depends on the size and number of vessels thrombosed As a rule only one major vessel is involved, and even if this is the main right or left pulmonary artery not more than half the total cross section of the pulmonary arterial tree is cut off and therefore pulmonary hypertension would not arise if the rest of the circulation were normal But the pulmonary circulation is never normal in these cases for otherwise neither the atherosclerosis nor the secondary thrombosis would occur The complication therefore nearly always has serious consequences In the congenital group with hyperkinetic pulmonary hypertension massive thrombosis may greatly elevate the pulmonary blood pressure overload the right ventricle and reverse the shunt In obliterative or vasoconstrictive pulmonary hypertension the relatively sudden increase of total pulmonary vascular resistance usually causes immediate right ventricular failure

Clinically massive thrombosis should be suspected in any advanced case of pulmonary hypertension of any type if there is relatively sudden deterioration in effort tolerance unexpected shunt reversal or unexpected heart failure Pulmonary thrombosis is never a dramatic event like massive pulmonary embolism and deterioration may be quite insidious in some cases As a rule the breakdown associated with thrombosis is subacute

rather than acute or chronic and the majority of cases are fatal (Magidson and Jacobson 1955)

The diagnosis may be confirmed by the skiagram which may show an exceptionally dense bulky pulseless comma shaped shadow in the position of one or other main pulmonary artery (fig 18 01) and an unduly translucent ischæmic lung distal to the block on one or other side (Keating *et al* 1953) Proof of the obstruction may be obtained by means of angio cardiography but this is rarely necessary



(a) 22nd March 1944



(b) 5th December 1946

Fig 18 01—Development of thrombosis of the right pulmonary artery in a case of anoxic cor pulmonale

*Subacute thrombo embolic pulmonary hypertension*

This is one of the most important forms of severe pulmonary hypertension for several reasons (1) socially and economically because it most commonly affects otherwise healthy young married women after childbirth (2) therapeutically because it can be cured by swift diagnosis and adequate treatment but is otherwise fatal (3) experimentally because it can be wholly reproduced and investigated in animal (4) academically because it is a most important and thoroughly understood link between simple obstructive pulmonary hypertension secondary obliterative pulmonary hypertension and so called primary pulmonary hypertension (*vide infra*) The disease therefore repays close scrutiny

Experimentally the condition has been reproduced in rabbits by repeated intravenous injection of finely fragmented fibrin clot

relatively large doses the rabbits died from heart failure secondary to obstructive pulmonary hypertension When the dose was nicely judged for the purpose however, the rabbits lived longer the emboli became organised, the lumens of the obstructed small arteries were reconstituted and the vessels were left with marked fibro elastic intimal thickening which was indistinguishable from that seen in primary pulmonary hypertension (Harrison 1948) This important work was confirmed by Barnard (1954) who produced similar lesions of the small arteries and arterioles of mice and rabbits by injecting thromboplastin into the systemic venous system so that fibrin emboli were formed *in vivo*

Physiologically pulmonary hypertension is initially obstructive then obliterative and finally may well be vasoconstrictive in response to the hypertension itself

Clinically cases present in a subacute manner with right ventricular failure secondary to severe pulmonary hypertension The majority are young married women and symptoms develop soon after childbirth occasionally the condition arises during pregnancy or is associated with some other cause of recurrent intravascular clotting of the appropriate kind Thus one of my five cases occurred in a young man following a sprained ankle small emboli being liberated from repeated phlebo thrombosis in the vicinity Death occurred within six months from right ventricular failure secondary to severe pulmonary hypertension Repeated small hæmoptyses were a feature of this case Of the other four two (a woman aged 40 and a man aged 36) followed simple recurrent thrombo phlebitis in the legs one of them died after a typical course lasting 18 months and the other is still alive on permanent anticoagulant treat ment The other two aged 27 and 25 were both associated with phlebo thrombosis following pregnancy One of them who appeared to be dying with advanced heart failure after inadequate treatment for two to three months was cured by prolonged anticoagulant therapy strict bed rest and intensive treatment for heart failure over a period of three months Final catheterisation in her case revealed complete restoration of the pulmonary vascular resistance to normal The other was progressing favourably with similar treatment for six weeks when she discharged herself from hospital because her husband did not appear to believe that she was seriously ill and needed her services at home At this time her pulmonary vascular resistance had fallen to 5 3 units (P A P 50/13 mm Hg C O 5 1 L/min ) and she had improved considerably in all other respects She has continued anticoagulant treatment as an out patient since and for a year has held her own but the clinical signs indicate that she still has moderate pulmonary hypertension

The case described by Castleman and Bland (1946) occurred in a woman of 35 following her third pregnancy she survived nine years of increasing obstruction and obliteration of the tertiary branches of the pulmonary artery the distal vessels remaining normal

The physical signs X ray and electrocardiographic appearances physiological findings course prognosis and detailed treatment of subacute thrombo embolic pulmonary hypertension are the same as for primary pulmonary hypertension (page 839) and will not be further considered here except to re emphasise the importance of prolonged rest and anti coagulant therapy the goal being a normal pulmonary vascular resistance It is not enough to prevent further embolism it may well be essential to keep the pulmonary blood pressure as low as possible for several months so that secondary proliferative changes and reactive pulmonary vaso constriction are discouraged Only when the resistance has fallen to normal should ordinary activities be resumed and pulmonary blood pressure lowering agents abandoned

*Subacute obliterative pulmonary hypertension*

The best examples of this condition are caused by periarteritis disseminated lupus and pulmonary schistosomiasis The first two have already been discussed to some extent in the section on cardiopathies of obscure origin and it is only necessary to add that both may cause obliterative pulmonary hypertension as a result of widespread arteritis involving the small vessels (Eskelund 1943) The clinical picture in this respect does not differ from any other kind of subacute pulmonary hypertension

*Schistosomiasis* has been recognised as a cause of pulmonary hyper tensive heart failure in Egypt for over twenty years (Azmy 1932) Either intestinal bilharziasis due to S Mansoni or urinary bilharziasis due to S hæmatobium may be responsible (Shaw and Ghareeb 1938) Ova from S Mansoni only reach the lungs when sufficient cirrhosis has developed to have resulted in anastomotic channels between the portal and systemic venous systems so that hepatosplenomegaly is invariably present in these cases ova from S hæmatobium can pass directly to the lungs The ova lodge in the arterioles, where they set up an acute obliterative necrotising arteriolitis, which is the cause of the pulmonary hypertension A specific angiomatoid lesion often develops in relation to capillary recanalisation of the occluded vessels (Shaw and Ghareeb 1938) Ova that escape through the wall of the arteriole cause the characteristic parenchymatous giant celled bilharzia tubercle (Sorour 1928) but these play no part in the syndrome under discussion Proximal to the sites of oval impaction the small arteries hypertrophy and develop marked intimal thickening—the usual reaction to pulmonary hypertension however caused

Clinically males are affected more often than females and the majority of patients are between 12 and 35 years of age Once pulmonary hyper tension has developed the clinical course and findings are like those of primary pulmonary hypertension (Bedford *et al* 1946) and death from congestive failure is likely within two years

A bedside diagnosis is usually possible as demonstrated by Kenawy (1950) It is based on (1) clinical features resembling those of

*Hypoxic pulmonary hypertension*

Pulmonary vasoconstriction which is not abolished by vagotomy or stellate ganglionectomy undoubtedly occurs in response to reduced alveolar oxygen tension both in animals (von Euler and Liljestrand 1946) and man (Motley *et al*, 1947) This response to oxygen lack is opposite to what occurs in the systemic circulation and has the advantage of deflecting the pulmonary blood flow from poorly ventilated zones (Liljestrand, 1948)

At first it seemed likely that this mechanism might be responsible for the pulmonary hypertension of anoxic cor pulmonale but it was soon discovered that the vasoconstrictive response seemed to occur only in acute experiments or clinical situations and was not maintained in the presence of chronic anoxia from advanced emphysema (Mounsey *et al* 1952) Nevertheless the reaction is clinically very important and explains why pulmonary hypertensive heart failure may be precipitated so easily by an attack of acute bronchitis in cases of chronic cor pulmonale and why oxygen therapy in such cases is so much more important than digitalis and elimination of sodium

## REACTIVE PULMONARY HYPERTENSION

This group characteristically includes all those cases with a high or extreme pulmonary vascular resistance that has developed in response to passive or hyperkinetic pulmonary hypertension (Wood 1952) e g pulmonary hypertensive mitral stenosis (page 540) 'false Bernheim's syndrome (page 774) and the whole of the Eisenmenger group (page 39?) but it may also include many cases in which pulmonary hypertension was caused initially by obstructive, thrombo embolic or obliterative vascular lesions and has been perpetuated by a similar reaction Whether or not hypoxic pulmonary hypertension is ever maintained long enough to be perpetuated in this way is uncertain but it is a possibility that should be borne in mind when attempting to synthesise the variable manifestations of cor pulmonale

The mechanism is not yet known for certain The belief that structural changes such as fibroelastic thickening of the intima of the small arteries and arterioles develop in response to passive or hyperkinetic pulmonary hypertension and gradually obliterate the pulmonary vascular bed and so cause secondary obliterative pulmonary hypertension is in the author's view untenable in the light of the known clinical and physiological data Evans (1951) went so far as to postulate a congenital deficiency of the media of the small pulmonary arteries in these cases and believed that fibroelastic thickening was a protective reaction which finally obstructed the pulmonary circulation and caused obliterative pulmonary hypertension

But it has been repeatedly pointed out that reactive pulmonary hypertension is *not* a late manifestation of mitral stenosis left ventricular failure patent ductus, ventricular septal defect or atrial septal defect but if

occurs at all it develops early pari passu with the critical passive or potentially hyperkinetic pulmonary hypertension caused by the lesions mentioned (Wood 1952 1954) This behaviour categorically denies that a secondary obliterative process is responsible for the initial reaction although it no doubt increases the already raised resistance as the years go by

Again it is nearly always possible to lower the pulmonary vascular resistance in cases of reactive pulmonary hypertension by injecting acetyl choline aminophylline or priscoline into the pulmonary artery and this would not be expected in obliterative pulmonary hypertension

Finally whenever passive or hyperkinetic pulmonary hypertension is relieved by surgical correction of the responsible lesion the pulmonary vascular resistance falls which does not harmonise with the mechanistic hypothesis

For these reasons it is believed that reactive pulmonary hypertension is due to active vasoconstriction, and that anatomical changes in the small pulmonary blood vessels are secondary, but such a mechanism awaits proof There is good evidence that neither an elevated pulmonary venous pressure chronic interstitial oedema an increased pulmonary pulse pressure dilatation of the pulmonary artery or alteration of the alveolar or blood gas tensions is responsible for the reaction The tentative hypothesis that in certain individuals pulmonary vasoconstriction develops in response to pulmonary hypertension itself (Wood 1952) fits the known facts best, and harmonises with the current theory that chronic essential hypertension in the systemic circulation may be initiated by any other form of systemic hypertension and once developed may be self perpetuating (Smirk 1949) If the hypothesis is correct reactive pulmonary hypertension should develop also in a proportion of cases of obstructive or obliterative hypertension which should then be perpetuated in the same way long after the initial cause has subsided The behaviour of certain thrombo embolic cases does not deny this possibility

Clinically reactive pulmonary hypertension in cases of mitral valve disease left ventricular failure and the Eisenmenger group has already been discussed in detail and will not be further considered here

## PRIMARY PULMONARY HYPERTENSION

There remains for discussion the enigma known as primary idiopathic or essential pulmonary hypertension

### *Incidence*

In a consecutive clinical series of approximately 10 000 cases of cardio vascular disease of all types personally examined by the author since the second world war there were 17 instances of primary pulmonary hyper tension (0 17 per cent) These were all diagnosed clinically in the first

instance all but two were confirmed by cardiac catheterisation and the ten that died (which include the two not catheterised) were confirmed at necropsy So far no case in which the final clinical diagnosis was primary pulmonary hypertension has been disproved by subsequent necropsy This should be enough to emphasise the highly distinctive nature of the syndrome and to re affirm that it is a disease entity in its own right whatever the cause

In my series there were 14 females and 3 males In Brenner s exhaustive analysis of the literature up to 1935 he could only find 16 convincing cases of primary pulmonary vascular sclerosis as it was then called but he did not give their ages or sex From my own files of the literature however I have records of another 20 acceptable cases making 27 in all although many more have been reported These include the cases of Brenner (1935) 1 Seely (1938) 1 de Navasquez *et al* (1940) 2 of their 3 East (1940) 3 Barrett and Cole (1946) 1 Gold (1946) 1 Gilmour and Evans (1946) 1 Rosenbaum (1947) 2 Dresdale *et al* (1951) 3 and Soulie *et al* (1955) 5 Of the total there were 28 females and 9 males This female preponderance may well prove important

The ages of these thirty seven patients ranged between 4 and 68, the average being 31 Four were children or adolescents twenty two were young adults between the ages of 20 and 40 eight were between 40 and 50 and three were over 50 Primary pulmonary hypertension in infants has also been described (Wolman 1950)

*Pathology*

Since Brenner s careful description the majority of authors have confirmed the great variability of the lesions Considerable dilatation of the pulmonary artery is almost invariable Atherosclerosis is common in the major arteries particularly in the older patients and is regarded as a secondary change secondary thrombosis may occur It is in the small arteries and arterioles that the most significant lesions are found these include fibroelastic thickening of the intima (Barrett and Cole 1946) a d hypertrophy of the media (Brenner, 1935) but normal vessels are nearly always seen as well and in several cases all the small vessels have looked normal (de Navesquez *et al* 1940 East 1940) McKeown (1952) moreover demonstrated that all the peripheral vascular lesions that have been reported as characteristic of pulmonary hypertension may be found in controls in the same age groups, which makes accurate interpretation very difficult

There are two other findings which must not be passed by Gilmour and Evans (1946) described hypoplasia of the media of many small vessels which they believed was congenital in origin and found that endarteritis fibrosa was closely related and presumably secondary to the defect In Gold s case (1946) there was also hypoplasia of the media and widespread secondary thromboses When old and new clots are a feature of the case

thrombo embolic obstructive hypertension with secondary obliterative changes is the more likely diagnosis

In my own cases the degree and extent of proliferative changes in the small arteries and arterioles was usually quite outside the range of what may be seen in controls but they could well have been secondary to the hypertension rather than its cause

*Physiology*

The high pulmonary vascular resistance imposes a heavy burden on the right ventricle which hypertrophies accordingly the right atrium gives maximum support and increases right ventricular diastolic stretch Despite these compensatory devices the cardiac output is low and on effort the right ventricle is readily overloaded (Howarth and Lowe 1953) so that the output may fall and result in syncope, whilst the reduced coronary flow may cause angina pectoris The arterial oxygen saturation remains normal until near the end and cyanosis is peripheral unless there happens to be a patent foramen ovale through which there may be a small reversed interatrial shunt

*Physiological measurements* were completed in 12 of my cases and were very similar to those reported by Dresdale *et al* (1951) *The pulmonary vascular resistance* averaged 15 units and ranged between 10 and 26 As Dresdale said this is about eight times the normal it is the same as is commonly found in fully developed reactive pulmonary hypertension in mitral stenosis and the Eisenmenger group

*The pulmonary systolic blood pressure* was well over 100 mm Hg (145 mm Hg) in only one instance in two cases it hovered round the 100 mark and in the rest it was only 65 to 90 mm Hg The diastolic pressure averaged 40 per cent of the systolic These unexpectedly low figures were attributed to right ventricular failure although at the time of catheterisation after treatment for congestive failure the right ventricular diastolic pressure was rarely much elevated Two of Dresdale s three cases also had pulmonary systolic pressures under 100 mm Hg

*The cardiac output* averaged 3 8 litres per minute in 11 adults and ranged between 2 6 and 4 5 at rest *The arterio venous oxygen difference* averaged 64 ml per litre the range being 56 to 80 Dresdale s figures were similar

*The arterial oxygen saturation* ranged between 88 and 95 5 per cent and averaged 92 per cent Each of Dresdale s cases was fully saturated

*Clinical features*

*Symptoms* include increasing effort intolerance due to fatigue, breathlessness angina pectoris or syncope Fatigue and breathlessness are forerunners of congestive heart failure Angina pectoris occurred of my cases and in two of 18 collected from the literature this incidence of 11 5 per cent syncope occurred in four of

and in four of 18 collected from the literature, i e in 23 per cent All my cases developed congestive failure, including those that are still alive

On examination the *physical signs* are highly characteristic and since they constitute the prototype of all kinds of pulmonary hypertension they are given here in full

1 Cyanosis when present is peripheral not central unless there is a reversed shunt through a patent foramen ovale which has been mentioned in necropsy reports in several instances The face may be highly coloured and bloated as in severe pulmonary valve stenosis but this is exceptional The hands are cold and blue as a rule unless hepatic failure causes vasodilatation and a palmar flush

2 The peripheral pulse is small

3 The rhythm is normal at first but towards the end paroxysmal or permanent atrial flutter or fibrillation is not uncommon in the more chronic cases

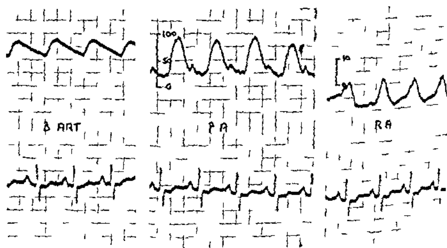



Fig 18 o.—Pressure pulse from the brachial artery pulmonary artery and right atrium in a case of primary pulmonary hypertension showing giant *a* waves in the right atrial tracing

4 The jugular venous pressure pulse reveals a giant *a* wave measuring 5 to 10 cm above it in three quarters of the cases (fig 18 o.) When there is advanced right ventricular failure the right atrium may also fail and the giant *a* may then disappear *v* becoming proportionately larger Functional tricuspid incompetence may also have this effect

5 Right atrial gallop rhythm and presystolic hepatic pulsation usually accompany the giant *a* wave

6 The left ventricle is impalpable but there is usually a powerful heave over the right ventricle between the left sternal border and mid clavicular

line Sometimes the right ventricle occupies the position of the apex beat Pulmonary artery pulsation was palpable in 60 per cent of my cases

7 There are five auscultatory signs right atrial gallop a tricuspid pan systolic murmur sometimes accompanied by a thrill when there is functional tricuspid incompetence (often heard well to the left since the dilated right ventricle occupies the apex beat) a sharp high pitched pulmonary ejection click over the dilated pulmonary artery a closely split second heart sound with sharp accentuation of the second or pulmonary element and a Graham Steell pulmonary incompetent diastolic murmur occasionally accompanied by a thrill in 40 per cent of cases An appreciable pulmonary ejection murmur is rare

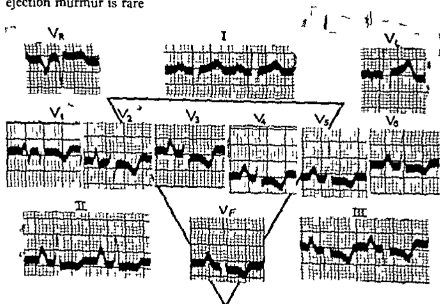



Fig 18 03—Electrocardiogram from a case of primary pulmonary hypertension showing a conspicuous P pulmonale and gross right ventricular preponderance

8 Signs of congestive heart failure are inevitable sooner or later

The *electrocardiogram* classically shows a conspicuous P pulmonale and gross right ventricular preponderance (fig 18 03)

X *rays* reveal a small aorta considerable *dilatation* of the pulmonary artery a variable degree of enlargement of the right ventricle and atrium an inconspicuous left ventricle and atrium and light peripheral vascular markings (fig 18 04)

*Cardiac catheterisation* reveals the physiological situation previously described If *acetylcholine 1 mg* is injected quickly into the pulmonary artery the pulmonary *vascular resistance falls* the pulmonary systolic and diastolic pressures fall the cardiac *output* rises (by 20 per cent in the case illustrated) the systemic blood pressure rises, and the heart rate

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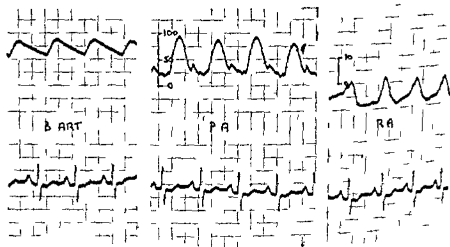



Fig 18 02—Pressure pulse from the brachial artery pulmonary artery and right atrium in a case of primary pulmonary hypertension showing giant *a* waves in the right atrial tracing

4 The jugular venous pressure pulse reveals a giant *a* wave measuring 5 to 10 cm above *v* in three quarters of the cases (fig 18 02) When there is advanced right ventricular failure the right atrium may also fail and the giant *a* may then disappear *v* becoming proportionately larger Functional tricuspid incompetence may also have this effect

5 Right atrial gallop rhythm and presystolic hepatic pulsation usually accompany the giant *a* wave

6 The left ventricle is impalpable but there is usually a powerful heave over the right ventricle between the left sternal border and mid clavicular

reflexly (fig 18 05) The advantage of using acetylcholine in these studies is that in the dose used it is virtually inactivated by the time it reaches the systemic circulation and therefore has a selective action on the pulmonary vessels The effect is immediate begins with the first heart beat following the injection and proves conclusively that some degree of vasoconstriction whether physiological or pathological is present in these cases if anatomical obstruction of more than two thirds of the total cross section of the pulmonary vascular bed is in fact present, then the relatively healthy vessels are maintaining disadvantageous vasoconstrictor tone alternatively the high resistance is due at least in part to abnormal functional vaso constriction

*Differential diagnosis*

Clinically the diagnosis of severe pulmonary hypertension secondary to a high pulmonary vascular resistance is usually obvious the only question at issue being whether it is primary obstructive obliterative or reactive and at the bedside this may not be answered at all easily If the onset of symptoms follows pregnancy phlebothrombosis a surgical or dental operation or an accident thrombo embolic obstructive or secondarily obliterative pulmonary hypertension is more probable if indeed this is not the cause of all cases Disseminated lupus periarteritis and schistosomiasis should be considered and tell tale clues searched for In primary pul monary hypertension all laboratory tests are negative

Reactive pulmonary hypertension due to mitral stenosis is probable if there is a history of rheumatic fever or chorea if the mitral first sound is sharp if a faint opening snap can be heard or recorded phonocardio graphically if slight dilatation of the left atrium can be demonstrated radiologically or if the electrocardiogram shows a P mitrale No difficulty of course arises if the classical signs of mitral stenosis are not masked by the large right ventricle In one of the author s cases the only clinical evidence of mitral stenosis was slight calcification of the mitral valve but this was considered conclusive and successful mitral valvotomy was carried out

Reactive pulmonary hypertension associated with patent ductus ven tricular septal defect or atrial septal defect is at once suggested if there is any direct or indirect evidence of central cyanosis or reduced arterial oxygen saturation at rest or on effort whether generalised as in atrial septal defect and ventricular septal defect or chiefly confined to the lower half of the body as in patent ductus In adults the history alone usually proves the congenital nature of the disease but in acyanotic children the differential diagnosis may not be ea y at the bedside Giant a waves however deny an alternative route for blood ejected from the right ventricle and therefore exclude patent ductus and ventricular septal

A loud pulmonary ejection murmur is much in favour of one Eisenmenger group in which the pulmonary blood flow aver

that in primary pulmonary hypertension A pure single second heart sound favours Eisenmenger's complex proper (with ventricular septal defect) and a relatively widely split second sound favours pulmonary hypertension with atrial septal defect Any clinical electrocardiographic or radiological evidence proclaiming a state of balanced ventricular work at once denies primary pulmonary hypertension and is strongly in favour of patent ductus or ventricular septal defect with reactive pulmonary hypertension

When in doubt the correct diagnosis may be established in most cases by means of cardiac catheterisation with or without the help of Evans blue or other dye Angiocardiography may also prove the presence and site of a reversed shunt The simplest out patient test, however, is to see whether or not the arterial oxygen saturation falls on effort this may be detected by means of an ear oximeter in cases of Eisenmenger's complex and pulmonary hypertension with reversed interatrial shunt and by means of femoral artery samples in cases of pulmonary hypertension with reversed aorto pulmonary shunt through a patent ductus

*Course*

The average duration of life from the onset of symptoms in 20 fatal cases was 3 2 years *the range one month to 10 years It is not without significance* that so far no early case has yet been diagnosed It was at one time suspected that mass radiography might reveal an occasional early case but this has not proved to be so of 10 patients discovered to have unexplained dilatation of the pulmonary arc *for example* but who were *symptom free* and without abnormal physical signs cardiac catheterisation revealed normal physiology This persistent failure strongly suggests that the disease is subacute rather than chronic and so it would be if it were initially thrombo embolic in origin

*Treatment*

No effective treatment has yet been devised for primary pulmonary hypertension Dresdale (1951) suggested priscoline *but it has proved* valueless in my cases although when injected directly into the pulmonary artery in a dose of 10 mg it undoubtedly lowers the pulmonary vascular resistance as does acetylcholine and aminophylline I have tried oral priscol 25 to 50 mg t d s aminophylline 0 2 G t d s etophylate 0 5 G t d s and hexamethonium bromide 500 to 750 mg t d s before meals all without the slightest effect I have also tried permanent anticoagulant therapy with dindevan on the chance that recurrent thrombo-emboli m was responsible but without avail Cortisone merely aggravated heart failure as a result of sodium retention and prednisone proved little less harmful in one case in which it was tried for several months In desperation on one occasion Blalock's operation of subclavian pulmonary artery anastomosis was attempted in the hope of providing a safety valve for the

pulmonary circulation but the patient died of ventricular fibrillation on the operating table

At the present time and in the light of what is known or suspected, there is a chance that a combination of strict bed rest or total inactivity, priscol theophylline and angolysen and permanent anticoagulant therapy may favourably influence a small number of cases which fulfil the clinical criteria for a diagnosis of primary pulmonary hypertension When heart failure is present it should be treated in the usual way

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CHAPTER XIX

# COR PULMONALE

*Definition*

The term cor pulmonale is best reserved to identify a specific cardiovascular disorder secondary to disease of the lung parenchyma although classically chronic it may be subacute or even acute

*Incidence*

It is difficult to estimate the prevalence of cor pulmonale for several reasons (1) the disease is rarely so labelled until there is congestive heart failure (2) its distribution is patchy apparently being more common in large industrial cities than elsewhere (3) in view of the frequency with which its clinical manifestations are precipitated by acute bronchitis or bronchopneumonia most cases are admitted to general hospitals rather than cardiovascular clinics and the recognition of cor pulmonale often depends a great deal on the interest of the physician concerned In the Registrar General s review for 1953 the disease is not listed at all as such but there were 30 392 deaths from bronchitis (6 per cent of the total mortality for England and Wales for that year) and 15 661 deaths from bronchopneumonia During the same year there were 61 751 deaths from ischæmic heart disease (12 per cent) 20 423 from hypertensive heart disease (4 per cent) and 8 837 from chronic rheumatic heart disease (1 8 per cent) Now in a general hospital in Sheffield according to Flint (1954) cor pulmonale accounted for 25 per cent of 300 cases of *congestive heart failure* ischæmic heart disease for 22 per cent hypertensive heart disease for 21 per cent and rheumatic heart disease for 23 per cent At the other extreme there is my own small series of only 45 proved cases of cor pulmonale amongst a consecutive series of about 10 000 clinical cases of cardiovascular disease of all types seen at specialised clinics and in private practice Realistic figures are therefore impossible to compile at the present time A reasonable conservative guess for the frequency of chronic cor pulmonale might be 5 to 10 per cent of all cases of organic heart disease

Cor pulmonale is at least five times more common in men than in women and about 75 per cent of the patients are over 50 years old (Spain and Handler 1946)

*Pathogenesis*

There are only two fundamental factors concerned with the development of cor pulmonale hypoxia and obliterative changes in the pulmonary

circulation The degree to which each contributes determines the clinical features and course of the disease Carbon dioxide retention may modify the symptoms but not the essential cardiovascular hæmodynamics

*Hypoxia* is commonly due to emphysema and is much aggravated by attacks of bronchitis bronchopneumonia and bronchial asthma which themselves are usually responsible for the emphysema The chief difficulty is ventilatory an insufficient number of alveoli are filled with fresh air at each breath Blood that perfuses unventilated alveoli cannot absorb oxygen or eliminate carbon dioxide The arterial oxygen tension therefore falls and the carbon dioxide tension rises in turn this results in reduced arterial oxygen saturation (McMichael and Sharpey Schafer 1944) and increased arterial carbon dioxide content (Taquini *et al* 1947)

Hypoxia however may also occur as a result of difficulty in oxygen perfusion across the alveolar capillary interface when the boundary zone is thickened in any way Carbon dioxide, being twenty five times more soluble in water than oxygen and therefore equally more diffusable, rarely experiences this difficulty so that in these cases hypoxia is *not* associated with carbon dioxide retention (Baldwin Cournand and Richards 1949) Arnott (1955) gives the chief causes of difficulty in oxygen diffusion as diffuse interstitial pulmonary fibrosis sarcoidosis silicosis inhalation of beryllium scleroderma radiation fibrosis and diffuse carcinomatosis

Hypoxia however produced results in central cyanosis vasodilatation an increased cardiac output (McMichael and Sharpey Schafer 1944) and polycythæmia *It is* the hypoxia that is responsible for the hyperkinetic character of the circulation in cor pulmonale During acute episodes of bronchitis bronchopneumonia or bronchial asthma the alveolar oxygen tension falls as a result of the increased ventilatory difficulty This causes transient pulmonary vasoconstriction (Motley *et al* 1947) further reduction in arterial oxygen saturation and a secondary rise of cardiac output in a group of cases described by Donald (1953) the mean pulmonary artery pressure rose from an average of 25 mm Hg to 50 mm Hg during such episodes This puts a heavy burden on the right ventricle which is asked to increase its stroke volume against an increased resistance and congestive failure is common

*Obliteration of a sufficient cross section of the pulmonary vascular bed* to raise the pulmonary blood pressure at rest is unusual in both emphysema and interstitial pulmonary fibrosis but there is frequently sufficient obstruction to cause obliterative pulmonary hypertension when the cardiac output is raised in response to effort or hypoxia (Bloomfield *et al* 1946 Harvey *et al* 1951) In my own series of 45 cases of well established cor pulmonale the pulmonary vascular resistance was between 6 and 10 units in 20 per cent and over 10 units (extreme) in a further 20 per cent but the arterial oxygen saturation in these two groups was no lower than in the 60 per cent of cases that had normal or only slightly raised resistances averaging 85 per cent at rest when free from infection and bronchospasm

irrespective of the resistance This lack of correlation is not surprising for the lower the arterial oxygen saturation the more the perfusion of un ventilated alveoli and this means non obliterated capillaries in the non functioning zones which would not encourage pulmonary hypertension Admittedly the pulmonary blood pressure may be higher in the more anoxic patients but this may be explained by the higher cardiac output

Whether or not the 20 per cent of cases with pulmonary vascular resistances *in the extreme range* have *reactive* vasoconstriction or merely advanced obliterative pulmonary hypertension remains to be seen Such a group would be expected if there is anything in the hypothesis propounded in the last chapter There is no doubt that secondary atherosclerosis thrombosis medial hypertrophy and fibroelastic intimal thickening may develop as a result of the long standing pulmonary hypertension and add their own obstructive or obliterative burden

*Clinical features*

The patient is usually a middle aged or elderly man He commonly gives a history of bronchial asthma or of recurrent winter bronchitis for many years with increasing breathlessness over the last year or two, and may have sought advice because of recent swelling of the legs Cross examination yields little further information he may have had attacks of tightness in the chest associated with breathlessness but not paroxysmal cardiac dyspnœa he may have had substernal discomfort, but not true angina he may prefer to be propped up a little at night but usually raises no objection to lying flat Headache attributed to a raised C S F pressure was noted in 55 per cent of Flint s series *Dyspnœa is attributed to oxygen lack* carbon dioxide retention (until the respiratory centre becomes insensitive) decreased pH and mechanically to the extra effort required to inflate and deflate the lungs (Christie, 1944)

In a minority of cases there may be historical clues pointing to the nature of the underlying lung disease e g symptoms of bronchiectasis established pulmonary tuberculosis pneumonectomy or thoracoplasty, Pott s disease of the spine or bronchopneumonia in the last London fog Cases with oxygen diffusion difficulty may give a history of severe and increasing breathlessness *on effort for which they have received scant sympathy* or they may mention occupational hazards of silicosis asbestosis or beryllium poisoning cutaneous or other lesions suggesting *sarcoid or scleroderma* deep X ray therapy for carcinoma of the lung or just a single attack of virus pneumonia Occasionally the onset of congestive heart failure is heralded by no previous symptoms whatsoever

*Physical signs*

Emphysema is usually obvious the chest is distended and moves little with respiration cardiac dullness is absent and the percussion note is generally tympanitic the breath sounds are faint Wheezing and r

denote bronchospasm or active bronchitis and the latter may also cause widespread coarse rales and mucopurulent sputum Central cyanosis may be gross or scarcely detectable It may be recognised in warm situations as in the conjunctivæ and inner sides of the lips where it is unlikely to be confused with peripheral cyanosis The hands are warm and the forearm veins distended capillary pulsation digital throbbing a modified water hammer pulse and increased pulse pressure may often be demonstrated (fig 19 01) Clubbing may occur but is unusual and pulmonary osteo

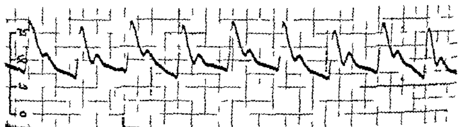


Fig 19 01 – Brachial arteriogram showing a typical waterhammer pulse in a case of anoxic cor pulmonale

arthropathy is more so Slight elevation of the jugular venous pressure and tachycardia may confirm the impression that the cardiac output is raised Papillœdema sometimes occurs and may be attributed to a raised C S F pressure associated with a greatly increased cerebral blood flow secondary to carbon dioxide retention (Simpson 1948)

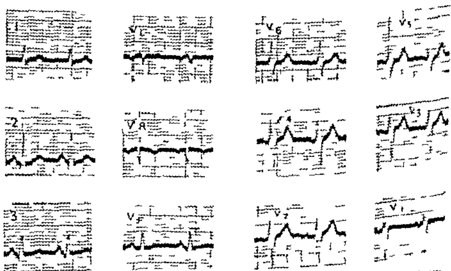


Fig 19 02—Electrocardiogram in a case of emphysema showing a vertical electrical position and clockwise rotation (viewed from below)

The heart itself is apt to be camouflaged by over expanded lung the apex beat is impalpable the left cardiac border impossible to locate by percussion the heart sounds difficult to hear and the second sound at the base often inaudible there are no murmurs but right sided summation gallop may be heard or felt just to the left of the sternum in the fourth intercostal space or in the epigastrium

When there is congestive heart failure the venous pressure is higher the liver distended and tender and œdema usually considerable the signs of a hyperkinetic circulatory state may remain or disappear gallop rhythm becomes diastolic in time and there may be functional tricuspid incompetence When the pulmonary vascular resistance is high in cor pulmonale the clinical findings are quite different, central cyanosis is still present but there may be peripheral cyanosis as well, the hands are cold and blue the forearm veins constricted, and there is no evidence of a hyperkinetic circulation, there may be a giant *a* wave in the jugular pulse and gallop rhythm is presystolic

In severe cases vasomotor collapse is apt to occur when some superimposed broncho pulmonary infection lowers the arterial oxygen saturation relatively suddenly the blood pressure drops the pulse becomes small and thready the cardiac output low and the skin cold and clammy the outlook is then very grave

*The electrocardiogram* Emphysema alone does not materially affect the electrocardiogram although it may cause clockwise rotation about the antero posterior and longitudinal axes (viewed from the front and below) Thus there may be right axis deviation in standard leads an RS pattern in lead $V_L$ a QR pattern in lead $V_F$ and an RS pattern from $V_1$ as far as $V_5$ or even $V_6$ (fig 19 02) When the heart is exceptionally vertical $V_R$ and $V_L$ may be indistinguishable or backward tilting of the apex may cause $V_L$ to resemble an œsophageal lead from the back of the heart

In 100 cases of chronic cor pulmonale analysed by the author (Wood 1947) the following electrocardiographic appearances were found *in standard leads* (fig 19 03a to e)

| | |
|---|---|
| Pulmonary P wave | 85 |
| Right axis deviation— | |
| with T3 (and often T2) inverted (a) | 20 |
| with T upright in all leads (b) | 30 |
| Prominent S wave in all leads (c) | 9 |
| Tendency to right axis deviation (d) | 11 |
| Normal axis of QRS (e) | 26 |
| Right bundle branch block | 4 |
| Low voltage | 40 |

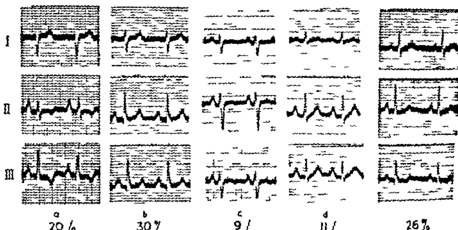



Fig 19 03—Standard lead electrocardiographic findings in 100 cases of cor pulmonale
(a) Right axis deviation with inversion of $T_3$ (and often $T_2$)
(b) Right axis deviation with upright T waves
(c) Dominant S wave in all standard leads
(d) Tendency to right axis deviation
(e) Normal QRS axis
The pulmonary P wave is seen in all

*Multiple chest leads* revealed the following (fig 19 04a to e)

| | |
|---|---|
| Normal QRS deflections in the majority (a and b) | |
| Inversion of T from $V_1$–$V_3$ (c) | 13 |
| Dominant R wave in $V_1$ with conspicuous S in $V_5$ (d) | 16 |
| Dominant S wave from $V_1$–$V_5$ (e) | 16 |

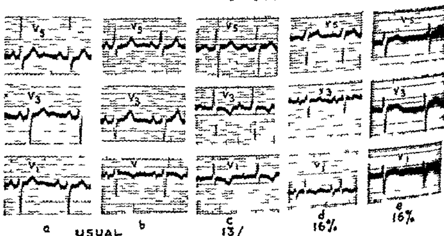



Fig 19 04—Chest lead findings in cor pulmonale
(a) (b) Normal chest leads
(c) Inversion of T from $V_1$ to $V_3$
(d) Dominant R wave in $V_1$ with conspicuous S in $V_5$
(e) Dominant S wave from $V_1$ to $V_5$





(a) (b)

Fig 19 05 (a) (b)—Skiagrams of two advanced cases of cor pulmonale showing dilatation of the pulmonary artery and of the left and right branches





(a) (b)

Fig 19 06 (a)—Right anterior oblique position showing the increased density and diameter of the pulmonary artery at its bifurcation

(b) Left anterior oblique position showing the left pulmonary artery forming an arc almost as dense and as large as the aortic arch

*Unipolar limb leads* nearly always showed a vertical electrical position. The pulmonary P wave is probably *the* earliest sign of cardiovascular disturbance resulting from emphysema or at least competes in this respect with elevation of the right ventricular pressure and slight reduction of the arterial oxygen saturation it may develop several years before the onset of heart failure

As would be expected the degree of right ventricular preponderance is proportional to the pulmonary artery pressure and pulmonary vascular resistance (Johnson *et al* 1950)

*Fluoroscopy* Prominence of the main branches of the pulmonary artery at the hila with or without dilatation of the main pulmonary arc is seen in over 50 per cent of cases of severe emphysema (Parkinson and Hoyle 1937) but the changes are rarely conspicuous until cor pulmonale is well advanced (fig 19 05 and 19 06) Associated hypertrophy of the right ventricle is less easily demonstrated

Pulsation of the pulmonary artery and its main branches may be seen sometimes but does not compare with that in atrial septal defect and as a rule is absent Peripheral vascular markings are relatively unimpressive Enlargement of the right atrium is rare in the absence of failure The left atrium is flat and a prominence on the left border of the heart between the pulmonary and left ventricular arcs is never seen Owing to the raised cardiac output and the average age of these patients the aortic knuckle is usually well seen and may be unduly prominent



Fig 19 07—Skiagram of a case of advanced anoxic cor pulmonale due to emphysema with a normal pulmonary vascular resistance showing a cardiovascular contour having no resemblance to the traditional descriptions

The changes described are not as frequent as originally supposed and are much more typical of the 40 per cent of cases that have a high pulmonary vascular resistance than of the 60 per cent that have not (fig 19 07) It is this unfamiliarity with the nondescript appearance of the cardiac shadow in many cases of advanced cor pulmonale with a raised cardiac output and normal resistance that has so often led to the diagnosis being overlooked Indeed when there is moderate coincident essential hypertension or ischæmic heart disease cases may actually present with left ventricular failure as in any other hyperkinetic circulatory state when the left ventricle carries the heavier load or is weakened by intrinsic

disease such cases are erroneously diagnosed as hypertensive or ischæmic heart failure

Then there may be evidence of emphysema widening of the rib spaces elevation of the ribs and clavicle depression of the diaphragm and increased translucency of the lung parenchyma However it is notoriously difficult to diagnose the degree of emphysema from the radiological appearances and in any case emphysema is not cor pulmonale

Finally X rays may reveal the nature of any underlying disease of the lungs that may be causing or behaving like emphysema such as bronchiectasis or honeycomb lung (fig 19 11) any of the diseases listed earlier that may cause interstitial fibrosis (fig 19 09) diffuse carcinomatosis (fig 19 10) or perhaps a surprise such as a massive bulla aneurysm or thrombosis of a main pulmonary artery (fig 18 01) As Flint (1954) pointed out pleural effusion is very uncommon in cor pulmonale owing to the frequency of obliterative pleurisy

*Special investigations*

The diagnosis of emphysema and its degree may be established by demonstrating static changes in the subdivisions of the lung volume namely a reduced vital capacity greatly increased residual volume or dead space diminished inspiratory capacity and a normal or increased total lung volume Typical findings were published by Whitfield *et al* (1951) as follows (for men)

| | *Normal controls (litres)* | *Moderate emphysema (litres)* | *Severe emphysema (litres)* |
|---|---|---|---|
| Vital capacity | 4 00 | 3 31 | 2 22 |
| Residual volume | 1 75 | 2 86 | 3 51 |
| Expiratory reserve | 1 27 | 1 05 | 0 70 |
| Inspiratory capacity | 2 73 | 2 26 | 1 52 |
| Total lung volume | 5 74 | 6 17 | 5 74 |

All workers in the field of emphysema however have found poor correlation between the degree of these changes and the grade of effort intolerance They are anatomical measurements and give little direct information about pulmonary function (Baldwin *et al* 1949)

The *maximum breathing capacity* is much reduced in emphysema and of course even more so when there is bronchospasm Over a 15 second test period of maximum respiratory effort only 20 to 30 litres per minute may be ventilated instead of the normal 75 to 100 litres per minute These low figures are due to mechanical difficulty in inflating and deflating inelastic emphysematous lungs and the reduced number of functioning alveoli It should be remembered that the maximum breathing capacity is an artificial test over a very short period of time and that normal subjects become dyspnœic when ventilating more than half their test figure

The *resting ventilation* (normally around 6 to 7 litres per minute) varies considerably according to the state of the blood gases the arterial pH and the sensitivity of the respiratory centre When the arterial $pCO_2$ and carbon dioxide content are high the respiratory centre is usually insensitive and respiration may be depressed in the presence of considerable anoxia Resting ventilation is more likely to be increased in emphysema when $CO_2$ retention is minimal and anoxia slight Much of the air inhaled is wasted in the increased dead space and unperfused alveoli or by over ventilation of relatively normal alveoli It follows that for each 100 ml of oxygen consumed more than the normal 2 5 litres of air must be breathed Thus the *ventilation equivalent for oxygen*, as this relationship is called is increased

*Ventilation on effort* is limited by mechanical respiratory difficulty It is usually expressed as a percentage of the maximum breathing capacity (Cournand and Richards, 1941) Patients with emphysema tend to develop very high ratios and complain less when the figure is over 50 per cent than patients with other respiratory diseases (Baldwin *et al* 1949)

*Mixing efficiency* is impaired in emphysema (Meneely and Kaltreider, 1941) If an inert gas like helium is inhaled it should reach all parts of the lung quickly and uniformly and the curve of its dilution should be rapid and uniform until mixing is complete In emphysema complete mixing is delayed for it takes longer for helium to reach the unventilated alveoli

The volume of the *poorly ventilated space* in emphysema can also be measured by the helium method and increases with the degree of emphysema

*Analysis of the blood gases* is the most important single measurement of the degree of emphysema Baldwin *et al* (1949) recognised four grades of severity in mild cases the arterial oxygen saturation was over 92 per cent at rest and did not fall on effort in moderate cases it was over 92 per cent at rest but fell on effort in grade 3 there was carbon dioxide retention in addition to a reduced arterial oxygen saturation at rest and in grade 4 there was heart failure in addition

Cor pulmonale only occurs in the two severe grades of emphysema and the average *arterial oxygen saturation* in my own cases was 85 per cent at rest This explains why central cyanosis is so often borderline The *arterial carbon dioxide content*, normally 44 to 53 ml per cent ranged between 62 and 71 vols per cent in a group of cases with heart failure studied by Platts and Whitaker (1954) More sensitive than measurement of the arterial oxygen content is that of the partial pressure of oxygen in arterial blood for this determines the quantity of oxygen that must combine with hæmoglobin The normal *arterial* $pO_2$ is about 100 mm Hg This may fall to as low as 62 while the *arterial oxygen* has only dropped to 90 per cent as the familiar oxyhæmoglobin dissociation curve shows (fig 19 08) Something is gained also by measuring the *arterial* $pCO_2$, for although a 5 per cent increase of CO tension results in approximately

a 5 per cent ri e of carbon dioxide content pCO is normally fixed close to 40 mm Hg so that quite small alterations are significant whereas the normal range of carbon dioxide content varies through 10 vols per cent from 44 to 53

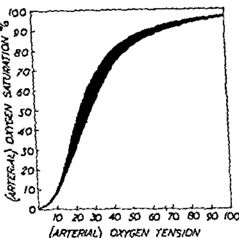



Fig 19 08—Composite oxyhaemoglob n dissociation curve (after Barcroft)

Again the $CO_2$ content of arterial blood is more helpful than the $CO_2$ *content of venous blood* the normal range for the latter varying between 53 and as much as 75 vols per cent

*The plasma pH* normally 7 41 is usually lowered in severe emphysema with cor pulmonale and ranged between 7 29 and 7 39 in the group of cases studied by Taquini *et al* (1947)

Finally estimation of the *alveolar capillary or alveolar arterial oxygen tension gradient* may give valuable information concerning oxygen diffusion across ventilated alveolar capillary membranes or the degree of perfusion of unventilated alveoli (venous admixture) High alveolar capillary oxygen tension gradients are characteristic of diffuse interstitial fibrosis (Donald *et al* 1952)

*The pulmonary blood pressure and cardiac output* may be measured by means of cardiac catheterisation Circulatory changes are unlikely to be present however unless the arterial oxygen saturation is below 92 per cent at rest and the arterial carbon dioxide content above 53 vols per cent When the pulmonary vascular resistance is normal or under 5 units the cardiac output is then raised but rarely above 10 litres per minute (McMichael and Sharpey Schafer 1944) When the resistance is high however the output is usually normal or even low Thus when both types are analysed together the net result is usually a high normal output around 6 litres per minute at rest

When pressures are normal at rest they may yet rise smartly on effort (Riley *et al* 1948)

*Diagnosis*

The usual cl nical problem is to decide whether the cardiovascular system is involved in a known case of emphysema this is not at all difficult for it is simply a matter of deciding whether the arterial oxygen tension and saturation are reduced and whether or not the pulmonary blood pressure is raised If central cyanosis cannot be recognised the arterial oxygen saturation is not likely to be below 85 per cent If the oxygen

tension is down there should be good evidence of peripheral vasodilatation and a hyperkinetic circulatory state The ocular fundi may suggest carbon dioxide retention Signs of pulmonary hypertension should not escape notice If there is heart failure or simply œdema a diagnosis of cor pulmonale can usually be made with confidence under the clinical circumstances If there is any doubt blood gas analysis should resolve it

Difficulty may arise in distinguishing cor pulmonale from other cardiopathies and especially in unravelling a mixed etiology Other hyperkinetic circulatory states may have to be excluded particularly cirrhosis of the liver in emphysematous alcoholics but also thyrotoxicosis secondary carcinomatosis of the liver and Paget s disease of bone in emphysematous subjects The commonest mixed etiology is the association of emphysema and hypertension Although the differences between hypertensive heart failure and cor pulmonale are many it should be remembered that both may occur at the same time

In the stage of low blood pressure and reduced cardiac output clinical diagnosis may be more difficult Toxic vasomotor collapse from bronchopneumonia may cause confusion mitral stenosis Pick s disease mediastinal tumour the Eisenmenger group other forms of severe pulmonary hypertension and many other conditions may have to be considered The correct diagnosis can usually be made after full investigation but the first clinical impression can be misleading

*Complications*

Pulmonary hypertension a raised cardiac output the effects of a high C S F pressure polycythæmia pulmonary osteoarthropathy insensitivity of the respiratory centre carbon dioxide narcosis and a number of other features that might be considered as complications have all been treated as part of the disease itself Similarly the absence of angina pectoris rhythm changes pleural effusion phlebothrombosis have also been referred to *Congestive heart failure* however requires further comment

It has already been explained that heart failure may result from over work (pulmonary hypertension and raised cardiac output) under hypoxic conditions According to Boniface and Brown (1953) a high carbon dioxide *tension also depresses myocardial function* There is however another important aspect of these cases that has been a source of much confusion— the effect on the circulation of a diminished renal plasma flow and diminished glomerular filtation This renal factor may come into play when the cardiac output is raised or well within the normal range (Lewis *et al* 1952) and causes sodium retention an increased blood volume (which masks polycythæmia) a rise of venous pressure and œdema when the heart is not overloaded On several occasions patients in this physiological state referred to the clinic because of heart failure have responded to physiological tests such as tipping and the Valsalva manœuvre like normal controls What constitutes heart failure proper and what does

not is largely a matter of definition but from the prognostic point of view the outlook is better in these cases than when the heart is overloaded

*Prognosis*

The diagnosis of chronic anoxic cor pulmonale usually carries with it a grave prognosis few cases surviving two years, but such diagnoses are rarely made before the onset of failure With the newer methods of investigation circulatory involvement should be recognised much earlier, perhaps by five years and appropriate treatment might then prolong life

*Treatment*

Vigorous preventive and symptomatic treatment of bronchitis and asthma may delay the development of serious emphysema indefinitely Half hearted measures must be condemned when the ultimate fate of these patients is realised

By the time the cardiovascular system is involved emphysema is usually far advanced A partly reversible state may be encountered however when acute bronchitis bronchopneumonia or an asthmatic bout is superimposed on chronic changes of only moderate degree In such cases infection should be treated promptly with penicillin or other forms of chemotherapy and bronchial spasm relieved by a dust free atmosphere and antispasmodics

Although details of such treatment cannot be considered in a work of this kind one or two observations are necessary Morphine is frequently lethal owing to its depressing effect on respiration pethidine may quieten a restless patient just as well is a good antispasmodic and does not depress respiration Subcutaneous adrenaline is still the most effective way of relieving bronchial spasm in an emergency newer remedies such as the anti histamine drugs may be given in addition but not as a substitute Isopropyl *nor* adrenaline which may be administered in sublingual tablets in doses of 20 to 40 mg is a useful preparation Antispasmodics that improve the cardiac output or coronary circulation such as aminophylline may be chosen in preference to those that do not An oral dose of 0 1 to 0 2 G t d s is usually insufficient and since repeated intravenous injections are impracticable and the intramuscular route too painful the only efficient way of giving aminophylline is by suppository 0 4 to 0 5 G twice daily Etophylate 0 5 G t d s or choline theophyllinate 0 5 G t d s however may be given by mouth as a substitute and etophylate is painle s intra muscularly

Whether the case is complicated by infection and bronchial spasm or not it is vitally important that the patient should be nursed in an oxygen tent The effect of improving the arterial oxygen saturation is often dramatic it prevents fatal vasomotor collapse reduces the cardiac output and may lower the pulmonary blood pressure The fear of carbon dioxide narcosis is no excuse for withholding the one remedy these patients need above all others It is true that some 10 per cent of patients with cor

pulmonale have developed such insensitive respiratory centres that they no longer respond to carbon dioxide but only to oxygen lack When oxygen is provided the increased arterial oxygen tension deprives the respiratory centre of its stimulus and respiration becomes depressed The arterial carbon dioxide tension may then rise very high indeed and the patient may become drowsy and finally lapse into coma (Davies and MacKinnon 1949) presumably with a high C S F pressure and cerebral œdema It is also true that oxygen is still given intermittently, but the fact remains that it is not given with sufficient enthusiasm nowadays, and patients are not recovering as quickly as they should in consequence As implied above 90 per cent of cases do not develop carbon dioxide narcosis when treated in an oxygen tent without any special precautions Moreover it has now been shown that the insensitivity of the respiratory centre is partly due to oxygen lack itself and may recover when oxygen is supplied (Westlake Simpson and Kaye 1955) Respiratory stimulants may also be given if drowsiness develops or an artificial respirator may be used Aminophylline may help and nikethamide may be given repeatedly in emergency Since aspirin may cause hyperventilation with secondary alkalosis by its direct action on the respiratory centre it has been tried recently in the cases under discussion (Wegria 1955) but since it also increases oxygen consumption by about 20 per cent (Tenney and Miller 1955) it is far from ideal

Mersalyl and a low sodium diet should be used with caution However McMichael and Sharpey Schafer (1947) have shown that in most cases with raised cardiac outputs the venous pressure is already at an optimum level and that lowering it by any means may *reduce* the output and harm the patient In a minority however the heart is overloaded and then responds to such treatment in the usual way Although clinically it may not always be easy to judge the physiological state of the circulation warm extremities and a full bounding pulse theoretically contraindicate all venous pressure lowering agents whereas cold extremities a small pulse and low blood pressure demand them (when the venous pressure is raised) When œdema is considerable and the jugular venous pressure over 7 cm above the sternal angle mersalyl and a low sodium diet should be tried Practical experience has proved their value and no harmful effects have been observed part of their usefulness is in removing what is virtually renal œdema

Venesection should certainly be avoided not only because its venous pressure lowering effect is too drastic and may be dangerous if ill judged but because correcting physiological polycythæmia results in a further increase of cardiac output a rise in pulmonary artery pressure and a fall in arterial oxygen saturation (Lewis *et al* 1952)

Digitalis or strophanthin may be used without fear if the heart is thought to be overloaded if in fact the output is raised and at its physiological maximum no harm will result from therapeutic doses

If, after relief of bronchial spasm and infection, the arterial oxygen saturation is still below 80 per cent when the patient is out of the tent antithyroid drugs should be seriously considered as a means of reducing the oxygen requirement (page 312)

## SPECIAL FORMS OF COR PULMONALE

*Diffuse interstitial pulmonary fibrosis*

In 1944 Hamman and Rich described a hitherto unknown type of parenchymatous disease of the lungs of uncertain etiology characterised by alveoli lined with cuboidal cells and separated from one another by marked proliferation of the interstitial connective tissue In this condition the physical barrier between alveolar air and capillary blood is considerable and efficient oxygen diffusion difficult Carbon dioxide being 25 times more soluble in water than oxygen has little difficulty in crossing the barrier This results in reduced arterial oxygen tension and saturation without carbon dioxide retention indeed hyperventilation due to anoxia may result in reduction of the arterial $pCO_2$ and carbon dioxide content The respiratory centre remains highly sensitive in this condition and responds vigorously to any rise in CO tension

The subdivisions of the lung volume maximum breathing capacity, mixing efficiency and poorly ventilated space may be altered very little though the increased rigidity of the fibrotic lungs may add to the work of respiration the inspiratory reserve capacity may be reduced and the intrapleural pressure swings greater than normal

Clinically these patients complain of severe dyspnœa at a time when little abnormal may be detected and on this account may receive scant sympathy an erroneous diagnosis of respiratory neurosis being made for in the early stages the X ray appearances of the lungs may be normal But the reduced arterial oxygen tension leads to early peripheral vasodilatation and the warm hands, throbbing digital vessel and distended forearm veins should not escape notice On effort the arterial oxygen saturation which may be over 90 per cent at rest drops sharply and central cyanosis may then be detected clinically

The diffusion difficulty may be demonstrated by measuring the alveolar arterial oxygen tension gradient which is much increased above the normal of 5 to 10 mm Hg serious venous admixture is excluded by relatively normal ventilatory function tests

As the disease advances the circulation becomes more hyperkinetic and cor pulmonale with heart failure develops sooner or later as in the case described by Sloper and Williams (1955) Pulmonary hypertension has not been a feature of my own three cases but is said to develop sooner or later in most (Arnott 1955) Radiological evidence of the diffuse fibrotic change also becomes apparent as a fine reticular or ground glass appearance.

The prognosis and treatment are similar to emphysematous

pulmonale except that antispasmodics are not required and there is no danger of carbon dioxide narcosis

*Other types of interstitial fibrosis*

A very similar physiological situation may arise from any other disease that thickens the barrier between the alveoli and the capillaries of the lung Donald (1953) lists the following causes of serious diffuse interstitial fibrosis beryllium granuloma asbestosis scleroderma sarcoidosis reticuloses and interstitial pneumonitis, and Arnott (1955) adds radiation fibrosis silicosis and diffuse carcinomatosis

Although the nature of the etiological agent is obviously important and every effort should be made to identify it the development and course of cor pulmonale in each type follows the same familiar lines How often a serious diffusion difficulty accompanies chronic interstitial œdema in mitral stenosis and left ventricular failure is at present uncertain In figure 19 09 the radiological appearances in a case of interstitial fibrosis are illustrated This woman who was very breathless on exertion also had signs of mild mitral stenosis but cardiac catheterisation revealed a left atrial pressure under 5 mm Hg a mean pulmon artery pressure of only 13 mm Hg, a cardiac output of 4 1 litres per minute and an arterial oxygen saturation of 86 5 per cent The radiological appearances are not unlike those of chronic interstitial œdema *but* in view of the findings independent interstitial fibrosis seemed inescapable

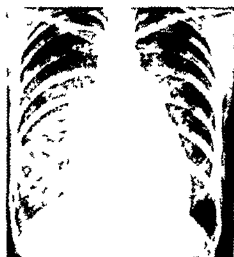


Fig 19 09—Diffuse interstitial pulmonary fibrosis in a case of mild mitral stenosis

*Cor pulmonale from pneumoconiosis*

Although many papers have described the frequency and course of cor pulmonale in pneumoconiosis (e g Coggin *et al* 1938 Thomas 1948) it is not yet clear whether emphysema interstitial fibrosis or obliterative pulmonary hypertension is chiefly responsible or whether a variable combination of all three factors are to blame Further detailed physiological studies are awaited with interest

*Diffuse carcinomatosis*

In previous classifications diffuse carcinomatosis has usually been regarded as a special form of subacute obstructive ' cor pulmonale when the term cor pulmonale included all forms of pulmonary hypertension

Two chief types were recognised (1) multiple embolic carcinomatosis behaving like subacute thrombo embolic pulmonary hypertension as in the case described by Mason (1940) which was secondary to carcinoma of the breast, (2) diffuse lymphatic carcinomatosis with secondary thrombosis of the small pulmonary arteries and arterioles as in the case described by Brill and Robertson (1937) in which carcinoma of the stomach was responsible

Of four cases of my own however none presented like subacute pulmonary hypertension but all had the features of subacute cor pulmonale with doubtful or absent central cyanosis at rest marked breathlessness and central cyanosis on effort, and a remarkably hyperkinetic circulation ending in congestive heart failure Only the last of these four was investigated physiologically and at the time clinical heart failure was present Both right and left atrial pressures were raised the right being 8/ 1 with reference to the sternal angle with *a* and *v* about equal in amplitude and the left being 15/5 with *v* dominant The pulmonary artery pressure was 45/20 the right ventricular pressure 45/0/8 the cardiac output 7 3 litres per minute the pulmonary vascular resistance only 2 units and the arterial oxygen saturation 83 per cent A low hæmoglobin (59 per cent) prevented central cyanosis at rest as it may often do in this group These findings excluded obstructive pulmonary hypertension At the time these four cases were seen it was not at all clear what was causing the central cyanosis for there was no evidence of emphysema There seems little doubt in retrospect that they were suffering from a diffusion difficulty and that physiologically they resembled cases with diffuse interstitial fibrosis The case investigated showed diffuse lymphatic spread from a bronchial carcinoma of the right middle lobe bronchus (fig 19 10) Of the other three cases the primary growth was in the stomach in one in the breast in one and was not established in the third



Fig 19 10—Subacute anoxic cor pulmonale with heart failure and a normal pulmonary vascular resistance due to diffuse lymphatic carcinomatosis secondary to bronchial carcinoma

Of four cases described by Storstein (1951) two were secondary to carcinoma of the stomach and two to carcinoma of the breast Physiological investigations in two of the cases revealed pulmonary artery pressures of 36/17 and 26/7 cardiac outputs of 5 and 4 litres per minute

pulmonary vascular resistances of about 4 and 3 units and arterial oxygen saturations at rest of 78 and 61 per cent respectively

Reporting 24 new cases of this condition and reviewing 154 from the literature Harold (1952) gives its frequency as 1 5 per cent of 836 con secutive necropsies at St Bartholomew s Hospital, or 7 5 per cent of all cases of malignant disease The essential pathological findings were distension of the peribronchial and perivascular lymphatics by tumour cells with secondary interstitial fibrosis intravascular tumour emboli secondary thrombosis and obliterative endarteritis were seen occasionally Of the total of 178 cases the primary tumour was gastric in 53 5 per cent bronchial in 13 per cent mammary in 9 5 per cent pancreatic in 6 per cent and prostatic in 4 per cent Although only one of Harold s 24 cases collected from the records at Brompton and St Bartholomew s Hospitals was recognised as having terminal subacute cor pulmonale his statement that the outstanding symptom was severe increasing breathlessness until the patient became distressed on the least exertion leaves little room for doubt as to what was happening physiologically It seems unlikely however that pulmonary hypertension was a feature of any of these cases

The clinical diagnosis is based on the combination of subacute hypoxic cor pulmonale usually without marked pulmonary hypertension the characteristic radiological changes of diffuse lymphatic carcinomatosis evidence of the primary neoplasm secondary anæmia instead of poly cythæmia relatively good ventilatory function absence of carbon dioxide retention and the demonstration of impeded oxygen diffusion

The prognosis is hopeless and treatment can only be symptomatic

*Honeycomb lung*

The occurrence of small thin walled air containing cysts measuring up to a maximum of 1 cm in diameter and widely distributed throughout both lungs may be associated with interstitial fibrosis however caused (Oswald and Parkinson 1949) Known forms of interstitial disease that may develop these cysts include xanthomatosis (Rowland 1928) reticuloses in infants (Mallory 1942) tuberous sclerosis (Berg and Vejlens 1939) and probably diffuse interstitial fibrosis itself (Oswald and Parkinson 1949) A few may be congenital Bronchograms reveal no filling of the cysts with lipiodol but the frequency of pneumothorax, which is often recurrent and bilateral suggests some communication between some of the cysts and the bronchial tree The cysts are sometimes lined with flattened epithelium sometimes not Adjacent cysts are separated by thick walled septa which may contain connective tissue and blood vessels The bronchial tree itself appears to be normal

Physiological studies in this group are scanty There were only two examples in my series of 45 cases of chronic cor pulmonale The first was a cyanosed woman of 26 with an obviously hyperkinetic circulatory state who finally developed congestive heart failure opened up a valve patent

foramen ovale, and died from paradoxical cerebral embolism Her vital capacity was 2 litre her arterial oxygen saturation 72 per cent in an oxygen tent and from the modest (grade 2) electrocardiographic changes her pulmonary vascular resistance was probably between 6 and 9 units

The second case was a man of 28 admitted with congestive heart failure and typical radiological evidence of honeycomb lung (fig 19 11) The arterial oxygen saturation was 69 per cent cardiac output 4 4 litres per minute mean pulmonary artery pressure 43 mm Hg pulmonary vascular resistance 10 units and hæmoglobin 115 per cent The arterial carbon dioxide content was not estimated

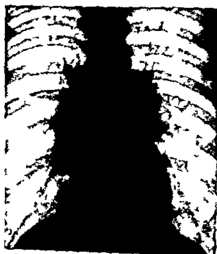


Fig 19 11—Anoxic cor pulmonale with a high pulmonary vascular resistance due to honeycomb lungs

Necropsy confirmed the diagnosis in both these cases but whether the physiological behaviour was like emphysema or interstitial fibrosis cannot be determined from the inadequate investigations carried out at the time

Clinically the majority of patients with honeycomb lung who survive the pneumothorax hazard develop cor pulmonale sooner or later Anoxia and a hyperkinetic circulation are probably usual but the pulmonary vascular resistance may also be high Interstitial fibrosis is likely to impede oxygen diffusion across the alveolar capillary interface and perfusion of unventilated air containing cysts is likely to cause a high degree of venous admixture in the arterial blood

*Ayerza s disease*

Much confusion has arisen from the use of this term it has been applied to cases of intense cyanosis and polycythæmia associated with syphilitic or other disease of the pulmonary arteries (Boyd 1931) The facts are that Ayerza of Buenos Aires *in an unpublished clinical lecture* (1901) described a single case of heart failure *in which* the patient was so cyanosed as to be almost black—a *cardiac negro* Autopsy revealed much enlargement of the right side of the heart dilatation of the bronchi and peribronchitis Neither syphilis nor the state of the pulmonary vessels was mentioned Arrillaga (1913 1924) was perhaps chiefly responsible for stressing the syphilitic origin of such cases although other authors from the Argentine believed the arterial lesions to be atherosclerotic Brenner (1935) after reviewing the evidence concluded that there was no goo

reason for retaining the term Ayerza s disease on the grounds that published cases described nothing but chronic cor pulmonale

*Cor pulmonale associated with deformities of the chest*

Gross kyphoscoliosis accounts for perhaps 2 5 per cent of cases of chronic cor pulmonale The condition is associated with extensive collapse atrophy of part of the lung and severe emphysema of the remainder Cardiovascular involvement is similar in type to that associated with other forms of emphysema kinking of the aorta (Corvisart) plays no part in its development*

A curious form of syncope has been described in a number (Chapman Dill and Graybiel 1939) possibly due to sudden lowering of the right atrial pressure consequent upon compression of the inferior vena cava in certain postures (page 13) Otherwise the symptoms are similar to those of cor pulmonale from ordinary emphysema There is al o the same tendency to chest infection

On the average death occurs five months after the onset of heart failure and at an average age of 30 years An injection of morphine is particularly lethal (Fischer and Dolehide 1954)

*Aneurysm of the pulmonary artery*

Aneurysm of the pulmonary artery is rare being found in less than 01 per cent of all autopsies and accounting for less than 0 5 per cent of all aneurysms (Deterling and Clagett 1947) The sexes are represented equally and about one third of the patients are under 30 years of age (Boyd and McGarack 1939) The etiology is believed to be a congenital defect in the wall of the pulmonary artery in about 40 per cent, syphilis in 30 per cent and chronic cor pulmonale with atherosclerotic pulmonary arteries in 30 per cent The diagnosis may be obvious on fluoroscopy if gross pulsation is seen if not it may be proved by means of angiocardiography (Robb and Steinberg 1940)

In pulmonary heart disease aneurysmal dilatation may develop remarkably quickly underlying congenital weakness of the arterial wall is difficult to exclude Thrombosis may occur in the sac or the whole vessel may be occluded but apart from such a complication the aneurysm is unlikely to influence the course of the primary disease Rupture is very rare

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CHAPTER XX

# THYROTOXICOSIS AND THE HEART IN MYXŒDEMA

## THYROTOXIC HEART DISEASE

THE cardiovascular system is clearly involved from the onset of thyrotoxicosis although the term thyrotoxic heart disease is usually reserved for the late stage when auricular fibrillation or congestive heart failure dominates the scene Such a distinction is artificial and simply means that a young and healthy heart can maintain a high output for years without distress but that an aged heart cannot

*Historical note* Thyrotoxic heart disease was first adequately described by Caleb Hillier Parry (1815 1825) of Bath who witnessed his first case in 1786 Flajani s publication of the details of one case (1802) appeared first but cannot be compared with Parry s account Graves description (1835) is also inferior Carl von Basedow (1840) a general practitioner at Merseburg Germany, called special attention to exophthalmos and drew a vivid picture of most of the features of primary exophthalmic goitre as we see it today omitting only tremor which was later recognised and added to the Merseburg triad (exophthalmos goitre and palpitations) by Pierre Marie (1883) For further historical details the reader is referred to the classical monographs of Cecil Joll (1932) and of Means and Richardson (1938)

### NATURE OF THYROID HORMONE

The exact composition of thyroid hormone is not yet known In 1895 Baumann obtained from thyroid tissue a protein free physiologically active substance containing 10 per cent of iodine which he called iodothyrin In 1899 Oswald showed that the active principle stored in the gland was attached to a protein in the form of thyroglobulin this is the chief constituent of colloid Kendall isolated thyroxine in 1915 showed that it contained 65 per cent of iodine and demonstrated its potency These researches culminated in the synthesis of thyroxine by Harington and Barger in 1927

Thyroxine however accounts for only 40 to 50 per cent of the total iodine in the thyroid gland is relatively insoluble and is not believed to be identical with thyroid hormone The rest of the thyroid iodine is found in the practically inert substance di iodotyrosine a likely precursor of thyroxine According to Harington (1933) thyroxine and di iodotyrosine are probably linked with amino acids as constituents of thyroglobulin in colloid and the natural thyroid hormone is perhaps a thyroxine containing peptide

*PATHOLOGY OF GOITRE*

The normal thyroid gland consists essentially of numerous acini lined with epithelium and containing colloid material rich in iodine from which thyroid hormone appears to be liberated according to the demand When the gland is stimulated the epithelium assumes an active columnar form and colloid tends to disappear When there is little or none left the walls of the acini may become crenated like any other vesicle whose contents have been removed In this phase the gland as a whole is soft and vascular and *is not enlarged When the stimulus ceases involution takes place* the epithelium flattens colloid reappears, and the acini become distended This is the resting phase and is characterised by a firmer less vascular gland of somewhat larger size If the stimulus to activity is excessive the morphological changes described above are supplemented by true hyperplasia of the acinar epithelium and subsequent involution may be incomplete leading to permanent enlargement of the gland

*Simple goitre* is due to benign hyperplasia and develops when iodine supplies are short or diverted especially when thyroid demands are heavy (Marine 1927) This response to iodine lack is believed by some to be mediated by the production of excessive amounts of thyrotropic hormone *from the anterior pituitary Endemic goitre due to* lack of iodine in the soil occurs in New Zealand parts of Italy and North America and in many other mountainous districts or places remote from the sea Iodine diversion may be due to polluted water (Marine and Lenhart 1910 McCarrison 1927) Increased demands for thyroid hormone occur at puberty and during pregnancy

*Colloid goitre* represents the resting involuted phase of previous benign hyperplasia (Marine 1930) When the stimulus subsides colloid reaccumulates in the acini intervening walls between distended crowded vesicles break down to form cysts and the whole gland becomes tense and big This process is innocent and causes no symptoms except possible discomfort in the neck

*In primary Graves disease* persistent uncontrolled stimulation of the thyroid gland of unknown cause leads to marked hyperplasia and to wild manufacture and liberation of excessive amounts of thyroid hormone The *acinar epithelium is columnar and proliferated* the walls of the acini markedly crenated and the colloid practically all gone The gland as a whole is soft vascular and enlarged

*Nodular goitre* is usually regarded as the end result of repeated cycle of hyperplasia and incomplete involution The process probably begins with failure of complete involution of a previously stimulated and hyperplastic gland Subsequent stimulation leads to local hyperplasia of these hypo involuted nests and subsequent involution to local nodules of colloid goitre Such a process may be repeated indefinitely Thyrotoxicosis from nodular goitre depends chiefly upon the activity of the hyperplastic nests the nodules themselves being mostly inert The term adenomatous goitre

is therefore incorrect when applied to this type of lesion and should be reserved to describe those cases in which thyroid nodules (usually single) are composed of solid masses of cells of fœtal type Compared with primary Graves disease nodular goitre usually runs a longer and less dramatic course which by its very nature is necessarily phasic periods of activity alternating with periods of relative quiescence Why production of thyroid hormone should exceed the demand is no more understood than it is in primary Graves disease The implication of the anterior pituitary thyrotropic hormone may explain part of the mechanism but in no way solves the problem

*Physiology of the circulation under the influence of thyroxin* The administration of thyroxin to man and mammals is followed after a time lag of several days by an appreciable rise in the basal metabolic rate The increased oxygen requirement is met by elevation of the cardiac output not by greater utilisation of available oxygen (as occurs when the B M R is raised by dinitrocresol) nor by polycythæmia The high minute output is maintained more by tachycardia than by a raised venous pressure the stroke volume being but little increased (Friedberg and Sohval 1937) The strength of cardiac contraction is probably enhanced These effects are usually attributed to the direct action of thyroxine on the heart

At the same time the peripheral blood flow is greatly increased there is obvious vasodilatation in the skin and adrenergic responses are magnified

*Morbid anatomy of the thyrotoxic heart* There are no macroscopic changes in the thyrotoxic heart prior to the onset of auricular fibrillation and failure until then the heart weight remains normal Cases exhibiting cardiac embarrassment during life may still show little at necropsy except some increase in heart weight and evidence of congestive failure (Kepler and Barnes 1932) In a few however there are scattered foci of fibrosis (Rake and McEachearn 1932)

## *CLINICAL FEATURES*

The hyperkinetic circulation of primary Graves disease is usually well tolerated because the subjects are young but in middle aged or elderly people with toxic nodular goitre cardiac embarrassment is the rule The sex ratio favours women in the proportion of about 6 1 (Fraser and Dunhill 1934) A family history of goitre is found in 45 per cent of cases (Bruun 1945) Contributory factors include pregnancy the climacteric infection (such as tonsillitis) and perhaps emotional shock although the scarcity of thyrotoxicosis amongst active service casualties in the first two world wars was noteworthy The role of iodine has already been discussed

Of the symptoms loss of weight heat intolerance agitation or restlessness palpitations and fatigue are the most important Loss of weight associated with a voracious appetite is particularly suggestive Palpitations may be due to vigorous and rapid action of the heart or to paroxysmal auricular fibrillation the latter is especially significant

Whilst the symptoms themselves are important the manner in which they are told and the general behaviour and appearance of the patient are often more so The subject is usually a woman she is commonly thin and talks quickly often gesticulating to lend emphasis to her remarks She may wear a scarf to hide an unsightly swelling in her neck but her clothing is otherwise light One of Parry s patients liked to sit in a draught stripped to the waist in order to keep cool (Parry 1815) A good moment to look for the goitre is towards the beginning of the interview when the patient may lean forward in her chair and swallow once or twice in nervousness The eyes are characteristic not so much because of exophthalmos which is usually absent but because of their typical stare The trend of the patient s conversation is often illuminating and in sharp contrast to that of the anxiety neurotic The latter complains of symptom after symptom in a challenging fashion exaggerating their severity and stressing his inability to cope with them The thyrotoxic patient tries to explain away her symptoms she feels the heat but of course it has been very warm recently she is losing weight but she supposes she was too fat before she gets tired and irritable but she knows she tries to do too much and so on

Physical examination may reveal a wealth of signs which are all directly or indirectly attributable to excess of thyroid hormone except exophthalmos and goitre They may be suitably described under four main headings

1 *The eyes* Exophthalmos may be present (fig 20 01) but is uncommon in toxic nodular goitre It is occasionally unilateral (fig 20 02) Artificial glass eyes may also become proptosed Its mechanism is still a subject of controversy (Zondek and Ticho 1945) but exophthalmos is certainly not due to sympathetic stimulation, for it is not relieved by sympathectomy (Shaw 1929) nor is it due to excess of thyroid hormone which never reproduces it Moreover exophthalmos occasionally becomes more marked after thyroidectomy or treatment with thiouracil In severe cases of exophthalmic ophthalmoplegia and malignant exophthalmos, thyrotoxicosis may be minimal and the protrusion of the eye ball appears to be secondary to intense œdema of the orbital contents (Brain and Turnbull 1938) Of great interest is the exophthalmos that can be produced in guinea pigs (also in rabbits and fish but not so far in man) by injecting thyrotropic hormone especially if the thyroid gland is first removed (Marine and Rosen 1933) All these facts point to the likelihood of the pituitary being directly responsible and provide further evidence that thyrotoxicosis may depend upon a primary pituitary disorder

Retraction of the upper lid (fig 20 03) revealing the white sclerotic above the iris (Dalrymple s sign), which may be unilateral is also uncommon in toxic nodular goitre It should be distinguished from exophthalmos which reveals the white sclerotic below the iris by mechanically displacing the lower lid (Pochin 1937-8)

If the patient looks up and then lowers the eyes to watch a descending object the upper lid lags behind the movement of the eye ball revealing



Fig 20 01—Exophthalmic goitre The first photograph (a) (in gipsy dress) was taken in 1933 the second (b) in 1936 The white sclerotics are seen below the iris due to mechanical displacement of the lower lid

(a)



(b)

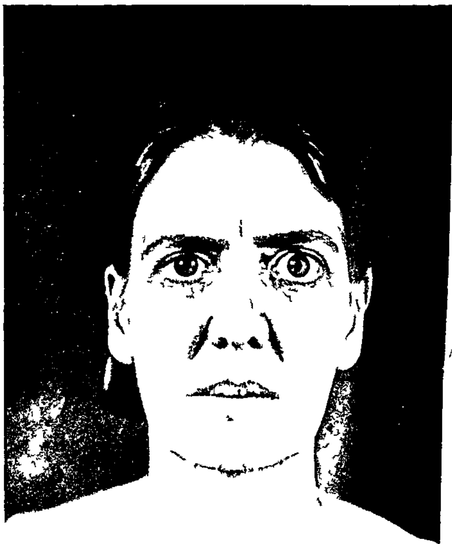


Fig 20 02—Unilateral lid retraction and exophthalmos



Fig 20 03—Lid retraction and characteristic thyrotoxic stare

the white sclerotic above the iris (von Graefe 1864) Lid lag and lid retraction were for a long time attributed to stimulation of the sympathetic reinforcement of the levator palpabræ superioris (von Graefe 1864) but if sympathetic stimulation were responsible the lower lid would also be retracted which it is not (Pochin 1937–8, 1939) Moreover, both exophthalmos and lid retraction may occur when the ocular sympathetic is paralysed (Brain 1939) In the light of these findings von Graefe s hypothesis is untenable

The characteristic stare has already been mentioned It is more than lid retraction and infrequent blinking (Stellwag s sign) it is a look which may occur independently and which can be recognised with experience The other eye signs of the textbooks are less important failure to wrinkle the forehead when the eyes are cast up (Joffroy s sign) may depend upon lid retraction and exophthalmos divergent strabismus as the eyes focus on an approaching object (Moebius sign) may be due to weakness of the oculomotor muscles as a result of stretching

2 *The hands* The hands are warm pink and slightly moist on both surfaces they are restless and expressive and may show a fine even constant tremor In contrast the hands of a psychoneurotic are cold and clammy being wet on the palms but not at the back they tend to be inert and expressionless tremor is coarse irregular and inconstant



Fig 20 04—Substernal goitre revealed by X rays

3 *The goitre* If a goitre is not seen it may be discovered by palpation It is best to stand behind the patient and to place the thumbs behind the sternomastoids and the fingers in front On asking the patient to swallow a nodular swelling may be felt moving upwards Posterior enlargement may be detected readily with this technique Practically all cases of thyrotoxicosis have a goitre although it is sometimes difficult to demonstrate (so called masked hyperthyroidism) In such instances it may become more convincing after a course of Lugol s iodine Occasionally it is substernal and may be revealed by fluoroscopy (fig 20 04)

The goitre of thyrotoxic heart disease is commonly nodular irregular and asymmetrical It may displace the trachea to one side and the common carotid artery to the other and on rare occasions it may compress the trachea causing cough dyspnœa and stridor Sudden enlargement is usually due to hæmorrhage within [illegible] or cyst Degenerated nodules may become calcified

Primary exophthalmic goitres are uniformly enlarged smooth and fleshy

They are similar to simple hyperplastic goitres but more vascular Some times an arteriovenous continuous thrill and murmur may be detected over the gland Colloid goitres are also smooth and symmetrical but they are harder and as a rule larger After a course of iodine primary exophthalmic goitre may feel like colloid goitre Nodular goitre should be distinguished from other causes of thyroid enlargement and from other swellings in the neck

*Fœtal adenoma* (Wolfler 1883) whether regarded as a true neoplasm arising in nests of embryonic epithelial cells or as an ordinary hyperplastic nodule in which the vesicles are unusually small and devoid of colloid (Joll 1932) presents clinically as a firm smooth single tumour within the sub stance of the thyroid gland It is usually innocent

What were believed to have been *malignant changes* were found by Wilson (1921) and by Speese and Brown (1921) in about 5 per cent of all goitres that were surgically removed but their histological criteria have been dis puted and the true incidence of malignancy is probably lower In non toxic goitres it may be between 1 and 4 per cent (Lerman 1944) but in toxic nodular goitre it is extremely rare Thus Means (1937) said he had not seen a single case and Crile (1936) met no instance of toxicity amongst 249 malignant cases Malignancy should be suspected when a goitre grows rapidly becomes unduly hard causes dysphagia involves the recurrent laryngeal nerve, surrounds and buries the common carotid artery obstructs the internal jugular vein causes pain by involving adjacent sensory nerves or when fixation can be demonstrated Enlargement of neighbouring cer vical lymph glands is particularly suggestive Metastases are found espe cially in the lungs and bone

*Riedel s disease* (Riedel 1896) may be readily confused with malignant disease clinically It is characterised by a brawny induration of part or all of the thyroid gland sometimes involving surrounding tissues It is a slow fibrotic process of unknown ætiology affecting individuals of either sex and of any age Pain dyspnœa dysphagia huskiness of the voice and obstruc- tion of neighbouring vessels occur and the gland is soon fixed but lymph nodes are not enlarged and thyrotoxic symptoms are unusual

*Lymphadenoid goitre* (Hashimoto s disease) is seen particularly in women over the age of 45 The whole gland is involved from the start surround- ing structures are not affected and myxœdema usually develops (Joll 1932) Microscopically acinar remnants are scattered among masses of lymphoid tissue

*Acute thyroiditis* may complicate a variety of infections but is rare It may be suppurative or non suppurative according to the nature of the in vading organism and to the severity of the attack Clinically it is charac terised by a painful tender uniform swelling of the gland accompanied by fever Cellulitis with or without suppuration may invade surrounding tis sues Thyrotoxic symptoms may be associated but usually subside with the inflammation

*Thyroglossal cyst* is essentially a mid line structure developing from remnants of the thyroglossal duct, and moves upwards when the tongue is protruded It is of cosmetic rather than medical significance

4 *Cardiovascular signs* Vasodilatation in the skin and muscle is nearly always present and may be recognised by hot extremities distended fore arm veins throbbing digital vessels capillary pulsation modified water hammer pulse and raised pulse pressure Tachycardia is the rule and persists during sleep (Boas, 1932) The action of the heart is vigorous the cardiac impulse being forceful and displaced a little to the left, and the heart sounds slapping A systolic murmur may be heard at apex or base and a thrill may be felt on compressing the carotid or subclavian artery Rarely a functional mitral diastolic murmur may be heard

Auricular fibrillation may be initiated by overdosage of thyroxine in patients with normal hearts It occurs in 10 per cent of all cases of thyro toxicosis and in 84 to 96 per cent of those with cardiac fail ure and may be paroxysmal or persistent It is rare in young subjects but becomes progress ively frequent with advancing years During attacks the ventri cular rate is apt to be very fast and the patient may complain of violent palpitations



Fig 20 05—Skiagram showing slight promin ence of the aortic knuckle and of the left pulmonary arc in a case of thyrotoxicosis

Cardiac enlargement and fail ure are also relatively late devel opments and are unusual with normal rhythm but often follow the onset of auricular fibrilla tion An appreciable proportion of such cases (over 50 per cent according to Magee and Smith 1935) are complicated by hyper tension or other forms of heart disease

X rays may show slight prominence of both the aortic knuckle and left pulmonary arc (Parkinson and Cookson 1931) and general fullness of all chambers probably due to the high cardiac output (fig 20 05) The electrocardiogram may be within normal limits unless it shows auricular fibrillation or the voltage of *P* and *QRS* may be aug mented (fig 20 06)

5 *Other and less constant features* Neurological signs are rare they in clude exophthalmic ophthalmoplegia and myasthenia—sometimes resem bling myasthenia gravis but not responding to prostigmine Curious-

patches of local myxœdema occasionally occur on the legs koilonychia has been described and the skin may be unduly pigmented

Decalcification of bone is not uncommon a negative calcium and nitrogen balance may be demonstrated the blood cholesterol may be rather low sugar tolerance may be reduced and impairment of hepatic function has been reported

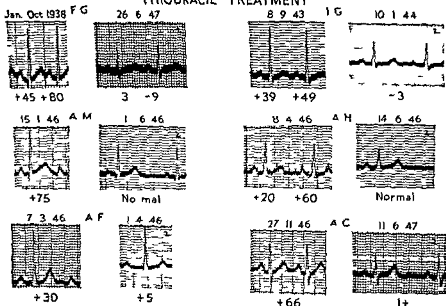



Fig 20 06—Ele trocardiog ams (all lead 2) showing relatively high voltage P and QRS waves in 6 ases of thyrotoxico is After *treatment* with thiouracil the voltage falls considerably The B M R is recorded und r each record

## SPECIAL INVESTIGATIONS

1 *The basal metabolic rate* (B M R ) introduced by Magnus Levy in 1895 has proved a useful guide to the degree of hyperthyroidism and is a measurement of the amount of oxygen consumed by the patient per minute when at complete rest i e fourteen hours after the last meal and after lying down undisturbed for at lea t half an hour The patient breathes in and out of a closed system containing equal proportions of air and oxygen for ten minutes carbon dioxide being removed by means of soda lime the amount of gas disappearing from the system represents the total amount of oxygen consumed This is then recorded in terms of oxygen consumption per square metre of body surface per minute and expressed as a percentage of what a normal person of the same age and sex would require In thyrotoxicosis, the B M R commonly ranges between plus 10 and plus 80 per cent Read s formula for estimating the B M R by the pulse rate and pulse pressure is unreliable and worth no more than the knowledge that the com

bination of tachycardia and a bounding pulse suggests a raised cardiac output (Read s formula is B M R equals ¾ [pulse rate plus ¾ pulse pressure] minus 72 )

It should be understood that a single B M R of plus 20 per cent does not necessarily mean that the disease is milder than one with a B M R of plus 40 per cent for the course of thyrotoxicosis is variable Serial readings may give a truer picture of the degree of activity Another important point is that auricular fibrillation and heart failure are more often associated with low grade activity acting over a long period of time, than with acute thyrotoxicosis so that the level of the B M R is no guide to the degree of cardiac disability

The B M R is more difficult to interpret when measured for diagnostic purposes but if it is below plus 10 per cent thyrotoxicosis is improbable High readings however may be due to faulty basal conditions or to other causes such as leukæmia and relatively high readings may be obtained in congestive heart failure of any etiology According to Foote *et al* (193 ) 23 per cent of thyrotoxic patients have basal metabolic rates within the normal range

2 *The administration of 10 minims* (0 6 *ml* ) *of Lugol s iodine* three times daily for a week or ten days may be used as a test for hyperthyroidism in two ways (1) to see whether it unmasks a goitre, for a hyperplastic gland enlarges and hardens under its influence (2) to determine its effect on the sleeping pulse body weight and B M R for these are beneficially influenced in thyrotoxic cases but not when the B M R is raised from other causes

3 *Measurements of the cardiac output peripheral blood flow and circulation time* provide valuable data Outputs of 8 to 12 litres per minute are usual and are correlated more with the heart rate than with the venous filling pressure When the heart fails the output drops usually to subnormal levels The fore arm blood flow is invariably increased and usually remains so when the cardiac output falls as a result of failure moreover the augmented flow does not subside for several weeks after the B M R has been restored to normal by means of thyroidectomy or thiouracil therapy (Howarth 1948) Circulation times under 10 seconds are characteristic (Goldberg 1938) and may remain well within normal limits when there is systemic congestion

The demonstration of a high cardiac output at rest places a case in the hyperkinetic group the differential diagnosis then includes severe anæmia anoxic cor-pulmonale arterio venous aneurysm Paget s disease of bone secondary carcinoma involving the liver or other serious hepatic disorders and beri beri The majority of these can be recognised or excluded at once on clinical grounds

4 *Urinary creatine test* Up to 200 mg of creatine may be excreted daily in the urine by normal women and children in an irregular manner but very little if any by normal men Excessive creatinuria occurs during

pregnancy and increased amounts may appear in the urine of either sex in fevers wasting diseases and certain muscular dystrophies

Most thyrotoxic subjects excrete an excess of creatine (Sohval King and Reiner 1938) and its detection may be used as a diagnostic test if the above considerations are borne in mind Thyroid responsibility may be proved by the disappearance of creatinuria within ten days of first giving iodine or thiouracil treatment (fig 20 07) (Schrire 1938) On the other

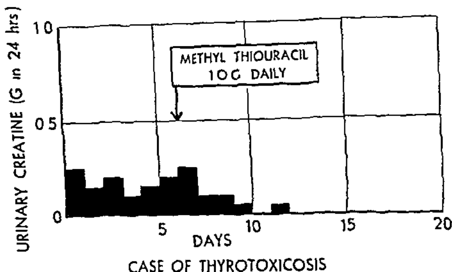



Fig 20 07—Effect of thiouracil on the excretion of creatine in the urine

hand, absence of creatinuria does not exclude thyrotoxic heart disease, for such cases are apt to be associated with low grade toxicity acting over a long period of time rather than with a high degree of hyperthyroidism and creatine excretion may be well within normal limits

5 *Electrocardiography* may reveal abnormally high voltage of P and QRS (fig 20 06) as previously stated It may also be of value in proving the nature of an irregularity of rhythm or in excluding certain other causes of a hyperkinetic circulation (e g pulmonary heart disease and anæmia)

6 *Radioactive iodine* ($I^{131}$) which has a half life of eight days may be given orally or intravenously in single test doses of 10 to 30 microcuries to see how the thyroid gland deals with it (Keating *et al* 1945) The body does not distinguish between radio iodine and ordinary iodine The concentration of $I^{131}$ in liquids such as the plasma and urine can be estimated by means of liquid counters that detect the beta ray emanation the concentration of $I^{131}$ in any tissue zone can be estimated by means of surface Geiger Muller counters that detect gamma rays which unlike the soft beta rays penetrate the skin Normally the concentration of $I^{131}$ in the thyroid gland reaches a maximum of about 33 per cent of the test dose in two or three days and then slowly declines (Myant and Pochin 19

Simultaneously *about 60 per cent of the test dose is excreted in the urine within two days*, the actual quantities extracted by the thyroid or excreted in the urine depending on the concentration of $I^{131}$ in the plasma The *plasma concentration necessarily falls to a very low level by the end of the* second day for 93 per cent of the test dose is by then in the thyroid gland or excreted in the urine Subsequently however $I^{131}$ again appears in the plasma as *protein* bound radiothyroxine The more active the thyroid gland the greater the quantities of iodine extracted and radiothyroxine manufactured the quicker the turn over and the less iodine excreted in the urine (Myant and Pochin 1949) the more inactive *the* gland the more does the reverse hold true

All radioactive iodine tests of thyroid function are based on these four fundamental principles

(i) *The concentration of $I^{131}$ in the thyroid gland* at the end of four hours in normal subjects averages 20 to 25 per cent of a 10 microcurie test dose (range 10 to 40 per cent) in thyrotoxicosis it is usually 40 to 90 per cent (Wayne 1954) This type of test is sometimes expressed as a *neck/thigh* ratio the concentration of $I^{131}$ in the thigh serving as a control so that the amount of iodine in the thyroid gland can be distinguished from the *amount in the soft tissues of the neck (Pochin 1950)*

(ii) Thyroxine as manufactured and released by the thyroid gland is closely bound to protein and when circulating in the plasma may therefore be precipitated with the plasma proteins Radiothyroxine of course is similarly protein bound As stated above the amount of protein bound radiothyroxine circulating in the plasma 24 to 48 hours after a 25 micro curie test dose of $I^{131}$ is negligible in normal subjects being less than 0 4 per cent of the test dose per litre of plasma at the end of 48 hours and usually less than 0 1 per cent (Goodwin *et al* 1951) in thyrotoxicosis however it ranges between 0 04 and 3 5 per cent per litre (Wayne 1954)

(iii) The *thyroid clearance* test is the best measure *of the speed at* which the thyroid gland extracts iodine from the plasma After an intravenous test dose of 30 microcuries of $I^{131}$ the thyroid gland normally extracts *about 6 per cent of the test dose per hour* when the plasma concentration is around 4 per cent of the test dose per litre this means that 1 5 litres of plasma are cleared of radio iodine per hour or that the thyroid clearance is 25 ml per minute *In* normal subjects the thyroid clearance ranges between 7 and 42 ml per minute *In* thyrotoxicosis however iodine extraction is speeded up and the thyroid clearance averages 240 ml per minute ranging between 80 and 500 (Pochin 1950)

(iv) *The quantity of $I^{131}$ excreted in the urine* is proportional *to its* concentration in the plasma provided renal function is unimpaired Normally over 40 per cent of a 10 microcurie test dose is excreted in 24 hours whereas in cases of thyrotoxicosis *less* than 25 per *cent* is usually excreted in this time (Pochin 1950) This test is an indirect measure of the amount of $I^{131}$ extracted by the thyroid gland during the 24 hours for the more

extracted the lower the plasma concentration and therefore the less excreted in the urine Mason (1949) and Fraser *et al* (1953) have shown that the urinary excretion test is more helpful if the amount of $I^{131}$ excreted during the first six or eight hours is considered separately for excretion is only diminished when the plasma concentration has fallen owing to increased thyroid extraction In practice the amount of $I^{131}$ excreted from the sixth or eighth to the twenty fourth hour after the test dose seems to be the most sensitive index of thyroid activity In normal subjects Mason (1949) found that 10 to 25 per cent of the test dose was excreted during the critical 6 to 24 hour period whereas in cases of thyrotoxicosis less than 4 5 per cent was excreted during this time

According to Wayne (1954) the most reliable of these tests is the estimation of protein bound radiothyroxine in the plasma at 48 hours thyroid clearance coming second and the amount of $I^{131}$ taken up by the thyroid gland in four hours third

*TREATMENT*

The most satisfactory method of treating thyrotoxic heart disease is subtotal thyroidectomy as developed by Dunhill (1908 1929 1937) The best results are obtained when physician and surgeon work in the closest harmony success depending as much upon the skill and judgment of the physician as upon the experience and dexterity of the surgeon (Fraser and Dunhill 1934) adequate premedication being all important

The patient should be put to bed and fed on a liberal and nourishing diet The addition of 5 to 10 mg of aneurin daily may be helpful on the grounds that an abundant supply of this vitamin is needed for the increased carbohydrate metabolism Fatigue and weakness may respond to 50 mg of pyridoxine daily (So kin and Levine 1944) Phenobarbitone ½ a grain (32 mg ) t d s or potassium bromide 10 grains (0 64 G ) t d s may also be prescribed with benefit and a nocturnal sedative is usually necessary

During this preliminary stage of treatment which usually induces some remission of symptoms the degree of thyrotoxicosis may be assessed clinically and by means of the special tests detailed above Prior to the introduction of thiouracil and the newer antithyroid drugs iodine was then given by mouth in doses of 10 minims (0 06 ml ) of Lugol s solution three times daily preferably in milk Within ten days there was usually marked improvement the pulse rate fell the B M R was lowered and the patient felt better (Waller 1914 Plummer 1923) The moment for operation was usually ten to fourteen days after beginning iodine Nowadays however preliminary treatment with antithyroid drugs is preferred (*vide infra*)

The introduction of thiouracil by Astwood (1943) following the discovery by the Mackenzies (1941) that the administration of sulphaguanidine to rats caused thyroid hyperplasia and reduction of colloid has proved an important therapeutic advance Thyroid hyperplasia was attributed to increased production of thyrotropic hormone by the anterior pituitary

endeavour to compensate for deficiency of thyroid hormone brought about by sulphaguanidine Astwood found that many substances had a similar effect including all the sulphonamides, p aminobenzoic acid thiourea and its compounds and that of these thiouracil offered the best prospects being potent and relatively non toxic It is held that thiouracil and the other substances mentioned act by interfering with the union of iodine and tyrosine and so prevent the formation of di iodotyrosine a known precursor of thyroxine (Riker and Wescoe 1945) The histological appearance of the thyroid gland under their influence resembles the hyperplastic gland of iodine deficiency

Since then several other more potent and less toxic antithyroid drugs have been developed and several of them have superseded thiouracil These include methylthiouracil propylthiouracil and neomercazole The initial dose of thiouracil and its derivatives is 50 to 100 mg three times daily for two weeks followed by 25 to 50 mg two or three times daily thereafter (Astwood 1949) Neomercazole (Lawson *et al* 1951) is in a different category the equivalent dose being only 10 mg two or three times daily initially and 5 mg once or twice daily for maintenance

Extensive trials have established what may be expected from treatment with antithyroid drugs (Astwood 1944 Williams 1944 1946 Himsworth 1948 Goodwin *et al* 1954) Amelioration of all symptoms except exophthalmos and those due to the size of the goitre and objective evidence of reduced thyroxine output can be demonstrated in 90 per cent of cases but when the drug is withheld after a year or so there is a 2 1 chance in favour of relapse within forty eight months (Goodwin *et al* 1954) Moreover toxic symptoms such as fever, dermatitis purpura, adenopathy and agranulocytosis which develop in 13 per cent of cases having thiouracil (Van Winkle 1946) prevent long term treatment even with the less toxic propylthiouracil or neomercazole in about 5 per cent of cases The mortality from agranulocytosis due to thiouracil is 0 5 per cent (Moore 1946) Increasing exophthalmos and the development of a highly vascular expanding goitre are attributed to over activity of the pituitary thyrotropic hormone in response to subnormal thyroxine output and may be prevented by the simultaneous administration of a maintenance dose of thyroid (Williams and Bissell 1943) or thyroxine (Fraser and Wilkinson 1953)

Despite the high relapse rate antithyroid drugs may be the treatment of choice in acute cases of primary Grave s disease in young people It is usually unsatisfactory in the long run in well established cases of toxic nodular goitre relapse in this group being more or less inevitable when the drug is withheld

The antithyroid drugs however have proved invaluable for preparing patients for partial thyroidectomy and if I thyroxine sodium 0 1 to 0 3 mg daily or thyroid gr 1 to 3 daily is given in addition increased vascularity of the gland can be avoided Lugol s iodine may be used

instead of thyroid for the same purpose (Means 1946) but is probably less efficient The great advantage of the antithyroid drugs over Lugol s iodine in preparing patients for operation is the abolition of the sense of urgency, for patients do not relapse while taking antithyroid drugs

Cardiac complications do not contraindicate partial thyroidectomy (Dunhill 1937) More careful preparation however is needed auricular fibrillation must be controlled and heart failure relieved before it is safe to operate but normal rhythm should not be deliberately restored at this stage

The commonest post operative complication used to be paroxysmal auricular fibrillation with rapid ventricular rate but this is less frequent if the patient is prepared with an antithyroid substance It should not occasion undue alarm for the rhythm usually reverts to normal spontaneously within 48 hours If auricular fibrillation persists however whether previously well established or of recent onset every effort should be made to restore normal rhythm by means of quinidine before the patient leaves hospital The risk of embolism is slight perhaps because the hyperkinetic circulation lessens the chance of venous thrombosis

*Treatment with radioactive iodine*

*Deep X ray therapy* was curative in about a third of cases resulted in some improvement in a third and was without benefit in the remainder (Means and Holmes 1923) In the treatment of thyrotoxicosis it has now been wholly superseded by radioactive iodine

*Radioactive iodine* introduced as a potent therapeutic agent by Hertz and Roberts (1942 1946) has fulfilled its early promise (Chapman 1948 Prinzmetal *et al* 1949 Moe *et al* 1950) Until a sufficient number of patients have lived 20 years after the irradiation the risk of subsequent carcinoma cannot be accurately assessed In the meantime all workers are disinclined to advocate it in patients under 45 years of age with a life expectancy of at least 20 years In older patients in subjects with other diseases that have a relatively poor prognosis such as V D H or ischæmic heart disease when thyroidectomy is refused or considered too dangerous or when thyrotoxicosis has recurred post operatively radioactive iodine is the treatment of choice An absolute contra indication however is pregnancy for the fœtal thyroid may concentrate $I^{131}$ and be destroyed or seriously damaged

The therapeutic dose of $I^{131}$ is approximately 100 to 200 microcuries per gram of estimated thyroid mass the exact dose depending upon the degree to which the gland concentrates radioactive iodine and the duration of its activity in the gland (Blomfield *et al* 1951)

The results of so treating 140 patients were reviewed after one year by Blomfield *et al* (1955) Symptoms usually abated within three to six months and finally 84 per cent became euthyroid myxœdema developed in 12 per cent and 4 per cent remained thyrotoxic There were no deaths

The thyroid gland usually became smaller in size and exophthalmos did not increase in the series reviewed (but may do so occasionally) The only side effect was rheumatism which occurred four to eight weeks after treatment in about 10 per cent of cases half of them non articular and recovering spontaneously

These results are impressive and certainly suggest that radioactive iodine would be the treatment of choice in all cases of thyrotoxicosis if the risk of subsequent carcinoma proves to be less than 2 per cent

*Thyrotoxic crises* Owing to the impossibility of neutralising thyroid hormone that has already been manufactured both iodine and thiouracil do not benefit the patient for several days (graphs illustrating the effect of partial thyroidectomy iodine and thiouracil on the basal metabolic rate are remarkably similar) The treatment of thyrotoxic crises by massive doses of iodine (by mouth or intravenously) as advocated by Boland and Kepler (1938) for example is therefore questionable Absolute rest heavy sedation and replacement of salt and water lost in sweating and vomiting are probably more important Aneurin, 100 mg. intravenously may also help *If toxic goitre is recognised and treated promptly however crises should not occur*

*Thyrotoxicosis and tonsillitis* Cases are encountered in which an attack or repeated attacks of tonsillitis are associated with thyrotoxicosis The problem then arises whether to perform partial thyroidectomy or tonsillectomy first Before the introduction of thiouracil most authorities agreed that it was safer to remove the thyroid gland before the tonsils for tonsillectomy in thyrotoxic patients sometimes precipitated a crisis Thiouracil has simplified the problem however and allows tonsillectomy to be undertaken first without risk



Fig 20 08—Skiagram showing gross cardiac enlargement in a case of thyrotoxicosis plus mitral stenosis

*Thyrotoxicosis and rheumatic heart disease* Thyrotoxicosis may be associated with acute rheumatic carditis or with established rheumatic valve lesions Both Parry's and Basedow's first cases were so related The association if more than a coincidence is indirect and may depend upon their joint relationship to streptococcal tonsillitis Rheumatic heart dis

ease with fixed valve lesions may result in enormous enlargement of the heart owing to the excessive work induced by thyrotoxicosis (fig 20 08) and the sooner the latter is treated the better Radioactive iodine is ideal for these cases

*Thyrotoxicosis and hypertension* There is a group of cases sometimes designated thyrotoxic hypertension in which thyrotoxicosis is associated with high blood pressure both systolic and diastolic levels being raised There is little evidence of any direct relationship between the two diseases and the blood pressure does not fall following thyroidectomy (Bisgard 1939)

*Thyrotoxicosis and angina pectoris* Ischæmic heart pain occurs when the blood supply to the myocardium is insufficient to meet the demand By increasing the demand thyrotoxicosis may induce angina in a patient with



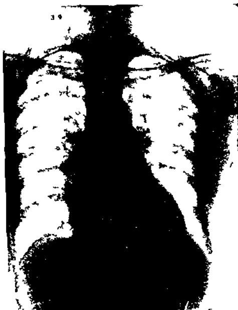


Fig 20 09 (a)—Thyrotoxic heart failure (b)—After subtotal thyroidectomy

a relatively minor degree of coronary atherosclerosis behaving in this respect like anæmia Thyroid hormone also sensitises the organism to adrenalin When ischæmic and thyrotoxic heart disease are associated angina may be completely relieved at least temporarily by successful treatment of the thyrotoxicosis preferably by means of radioactive iodine

*Thyrotoxicosis and pregnancy* Thyrotoxicosis developing during pregnancy may be due to primary exophthalmic or nodular goitre With the aid of thiouracil in combination with small doses of iodine or thyroid patients should be taken safely to term If the condition does not then subside subtotal thyroidectomy may be carried out The danger of goitre

developing in the fœtus is minimised by the iodine (or thyroid) but it is well to keep the dose of antithyroid drug as small as possible

## PROGNOSIS

There are few forms of heart disease that respond better to adequate treatment than thyrotoxic heart disease Cases with gross congestive failure and well established auricular fibrillation may be cured and the largest hearts may resume their normal size (fig 20 09) On the other hand heart failure and death are inevitable if the disease remains unchecked In the hands of the best surgeons the mortality rate of subtotal thyroidectomy in cases of toxic nodular goitre has been 1 6 per cent (Cole 1944) to 2 6 per cent (Dunhill 1937) but it may be less with thiouracil preparation No reliable figures are available upon which to assess the total relapse rate Post operative tetany and paralysis of the vocal cord each occurs in approximately 1 per cent (Means 1946)

Myxœdema which may follow otherwise successful treatment of thyrotoxicosis however accomplished is easily controlled by a maintenance dose of thyroid gr 3 or L thyroxine sodium 0 3 mg daily

## THE HEART IN MYXŒDEMA

Artificial myxœdema produced by total ablation of the thyroid gland or by antithyroid drugs benefits the heart by lessening the circulatory demands and so relieves angina pectoris and congestive heart failure Yet well developed myxœdema from natural causes gives rise to cardiac enlargement pericardial effusion and ultimately to congestive heart failure moreover angina pectoris may be associated Enlargement cannot be due to overwork it must depend upon some intrinsic change in the heart muscle Histological examination however, is usually disappointing The fault is probably biochemical and is unlikely to be properly understood until studies in tissue chemistry are more advanced

The diagnosis of myxœdema is suggested by the placid sleepy character (unless there is manic psychosis) poor memory sensitivity to cold (Raynaud s phenomenon is common) dry coarse skin thickened lips and tongue low thick voice baggy eyes scanty dry hair podgy hands supraclavicular pads of fat and general pallor It is confirmed by an impalpable thyroid gland by a B M R of minus 30 to 40 per cent by prolongation of the arm to tongue circulation time to 19 to 25 seconds by a high blood cholesterol of 300 to 400 mg per cent by relative insensitivity to atropine and adrenaline by a characteristic form of anæmia and by a pathognomonic electrocardiogram If further proof is needed it may be obtained by demonstrating failure of the thyroid gland to extract radioactive iodine after a test dose so that the neck thigh ratio remains unaltered (Foote *et al* 1957) a thyroid clearance of only 1 to 4 ml per minute (Pochin 1950) or an abnormally high urinary excretion of radio iodine (Mason 1949 Fraser *et al*, 1953) Estimation of the protein bound radiothyroxine 48 hours

after a test dose of $I^{131}$ does not distinguish myxœdema from normal controls (Wayne 1954)

The type of anæmia that responds to thyroxine alone is normocytic and orthochromic, and may be regarded as a compensatory adjustment to diminished oxygen requirement (Bomford 1938) The electrocardiogram shows sinus bradycardia low voltage atrial and ventricular complexes and flat or inverted T waves in all leads (fig 20 10) The cause of these changes is not yet understood they do not depend upon the presence of pericardial effusion nor upon the state of the subcutaneous tissues The response to thyroxine is quick and complete and accompanies beneficial changes in the B M R The electrocardiogram in cretinism behaves similarly (fig 20 11) (Schlesinger and Landtman 1949)

Whilst a well developed case of myxœdema is difficult to overlook (fig 20 12) cases of short duration especially in younger women (the sex incidence is 8 1 in favour of women) may easily escape notice The diagnosis should be considered in any case of congestive heart failure or of peri-

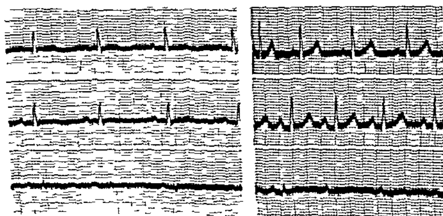
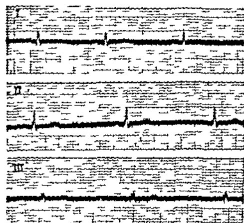


Fig 20 10 (a)—Electrocardiogram showing sinus bradycardia low voltage atrial and ventricular complexes and flat T waves in all leads in a case of myxœdema
(b) Normal electrocardiogram after treatment

cardial effusion of unknown etiology Congestion when it occurs is systemic and is associated with a low cardiac output Pericardial effusion is due to simple transudation Cardiac enlargement is general and pulsation of all chambers poor Angina pectoris has been said to occur in only 1 to 2 per cent of cases (Smyth 1938), but is surely much more frequent (Hueper 1944 1945) Coronary atherosclerosis may result from the high blood cholesterol Myocardial infarction without coronary thrombosis has been described in such cases when treated too vigorously with thyroxine The blood pressure is little influenced by myxœdema and is as often elevated as low When congestive failure is present measurements of the B M R give unduly high readings more reliance should then be on other tests, especially on the electrocardiogram



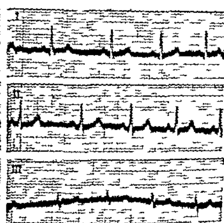



Fig 20 11—Electrocardiogram before and after treatment in a case of cretinism



Fig 20 12 (a)—Myxœdema



(b) After seven weeks treatment

*Treatment* If there is no evidence of coronary disease thyroxine may be given intravenously in a single dose of 10 mg or thyroid may be given by mouth in doses of 3 grains (0 2 G) daily The response is delayed but dramatic Within five to ten days the B M R rises the blood cholesterol falls the T wave begins to change and clinical improvement is obvious Signs of failure or of pericardial effusion soon disappear and the heart gradually resumes its normal size (Lerman Clark and Means 1933)

Initial treatment is easier than maintenance With the aid of the B M R it is not difficult to regulate dosage for a patient at rest in bed but when she leaves hospital and varies her activities it is not so easy and supervision is required for life The average maintenance dose of thyroid is 3 grains (0 2 G) daily by mouth or 0 3 mg of L thyroxine sodium

If there is any suspicion of associated coronary disease initial treatment should be cautious and the oral route advised Not more than 1 grain (65 mg) of thyroid should be given daily and in cases with angina pectoris not more than ½ a grain (32 mg) The dose may be increased slowly week by week if well tolerated or reduced and maintained at a minimum if not tolerated

The chief complication arising during treatment is the development of angina pectoris should this occur the dose of thyroid may have to be less than ideal but enough to keep the blood cholesterol below 300 mg per cent

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CHAPTER XXI

# HYPERKINETIC CIRCULATORY STATES

## (ANÆMIA PREGNANCY ARTERIO VENOUS FISTULA, BERI BERI PAGET S DISEASE OF BONE HEPATIC FAILURE)

IN addition to the diseases enumerated above hyperkinetic circulatory states (Harrison 1935) include thyrotoxicosis anoxic cor pulmonale fever and exercise The first two have been considered fully elsewhere and the last two have a purely physiological basis

All these conditions are characterised by a raised cardiac output main tained by means of tachycardia a raised venous filling pressure or both moreover the heart may beat more strongly Conspicuous evidence of vaso dilatation in skin and muscle is found in all of them the skin is warm and flushed the forearm veins are distended the pulse is bounding the digital vessels throb and there may be capillary pulsation The forearm and calf blood flows are increased Whilst young and healthy hearts may cope with the situation without distress older or unhealthy hearts may fail to meet the requirements The chief symptoms are palpitations and breathlessness

It may be difficult clinically to recognise congestive failure in these cases for the usual signs may have other interpretations Thus a raised venous pressure may be part of the physiological mechanism maintaining a high cardiac output (McMichael 1947) enlargement of the liver may be due to secondary carcinoma or to hepatitis and œdema is commonplace in severe anæmia and beri beri for other reasons Indeed it is by no means easy to be sure what is meant by failure in this group for example McMichael uses the term high output failure to describe a state in which a raised venous pressure and œdema are associated with a high cardiac output whether or not the latter is capable of being raised further Yet failure ordinarily denotes an overloaded heart or ventricle one incapable of raising its output further But this question has already been discussed (page 264)

## THE HEART IN ANÆMIA

*Physiology* Severe chronic or post hæmorrhagic anæmia may affect the heart in three ways (i) it may cause a hyperkinetic circulatory state as described above (ii) it may cause or precipitate angina pectoris or acute coronary insufficiency (iii) it may result in nutritional degenerative changes in the cardiac muscle which may reduce its reserve

With an oxygen consumption of 240 ml per minute an anæmic subject with a hæmoglobin of 20 per cent could not have a cardiac output less t[illegible]

6 litres per minute if all the available oxygen were utilised (20 per cent Hb = 3 G Hb per cent = 3 × 1 34 ml oxygen per cent = 4 ml oxygen per cent or 40 ml per litre Thus cardiac output $= \frac{240}{40} =$ 6 litres per minute) If half the available oxygen were utilised the cardiac output would be 1 litres per minute

In anæmic subjects investigations have shown that the resting cardiac output may reach 13 litres per minute and utilisation of available oxygen may be increased from the normal 33 per cent to as much as 90 per cent (Liljestrand and Stenstrom 1925–6 Nielson 1934 Sharpey Schafer 1944) These changes do not occur at rest with hæmoglobin values above 50 per cent but become increasingly apparent at lower levels (Bouchut and Froment 1934) The high cardiac output is maintained both by tachycardia and a raised venous pressure The latter must be due to widespread capillary or peripheral venoconstriction for the blood volume is reduced (McMichael *et al* 1943) and the small arteries and arterioles are dilated (McMichael 1947)

*Clinical features* The chief symptoms of severe anæmia are breathlessness fatigue and palpitations Angina pectoris occurs in about 30 per cent (Coombs 1926 Pickering and Wayne 1934) occasionally even when there is no underlying coronary disease Thus the author has treated a boy of 17 with pernicious anæmia and angina pectoris and also a young man of 21 who presented himself with classical ischæmic heart pain due to iron deficiency anæmia resulting from bleeding hæmorrhoids Œdema may be due to congestive heart failure but is more often nutritional It is especially prone to develop during the first three weeks of blood regeneration in response to treatment of the anæmia

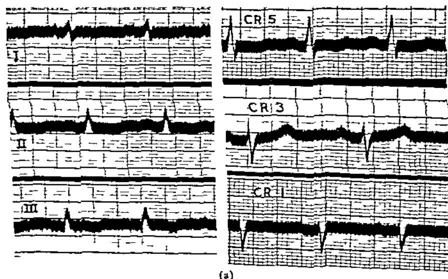
Paroxysmal cardiac dyspnœa or acute pulmonary œdema is rare as a spontaneous event but may arise during blood transfusion or saline infusion These procedures should not be lightly undertaken in cases of severe chronic or post hæmorrhagic anæmia precautionary measures include the use of concentrated red cells instead of whole blood and venous pressure lowering agents such as cuffs applied to the thighs Transfusion should be temporarily abandoned if the venous pressure is seen to rise appreciably

*Physical signs* A hyperkinetic circulation and peripheral vasodilatation may be recognised by the features detailed previously

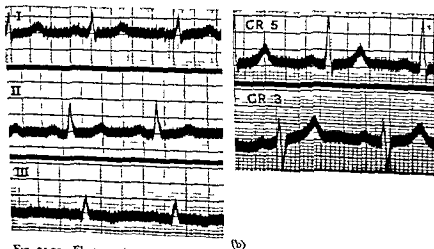
A functional systolic murmur (so called hæmic murmur) at apex or base is common and is due to the increased blood flow through the aortic and pulmonary valves Functional mitral or aortic diastolic murmurs may also be heard occasionally earlier observations such as those by Von Noorden (1891) Sahli (1895) and Kraus (1905) having been amply and repeatedly confirmed (Goldstein and Boas 1927) Mitral presystolic or diastolic murmurs are probably due directly or indirectly to the increased velocity of blood flow the mechanism being the same as that responsible for mitral

diastolic murmurs in patent ductus arteriosus ventricular septal defect and thyrotoxicosis Basal diastolic murmurs are attributed to dilatation of the aortic or pulmonary ring

*The electrocardiogram* Despite several publications emphasising the normality of the electrocardiogram in anæmia (e g Smith 1933 Pickering and Wayne 1934) there can be no doubt that significant changes occur in at least a third of cases with hæmoglobin values under 40 per cent (Block, 1937) In a consecutive series of twenty such cases analysed by the author




(a)




(b)

Fig 21 01—Electrocardiogram showing low voltage and flat or inverted T wave in all leads in a case of pernicious anæmia

(a) Before treatment

(b) After correction

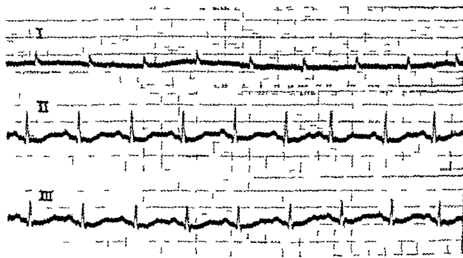



Fig 21 02 Electrocardiogram showing depression of the ST segment due to acute coronary insufficiency resulting from post hæmorrhagic anæmia

(a) Before treatment

(b) After treatment of the anæmia

Fig 21 03—Skiagram showing general cardiac enlargement in a case of severe pernicious anæmia

right showed low voltage depressed S T segments or flat or inverted T waves in left ventricular surface leads or their equivalents As the anæmia improved under treatment these faults were corrected (fig 21 01) Several instances of bundle branch block have also been observed but these have always persisted when the anæmia was cured Depression of the S T segment is common following gross hæmorrhage and is believed to represent temporary coronary insufficiency (fig 21 02)

*Fluoroscopy* X rays often reveal slight enlargement of all chambers of the heart and prominence of both the aorta and pulmonary artery in cases with hæmoglobin levels below 40 per cent (fig 21 03)

Necropsy studies have revealed slight increase of heart weight (350 to 450 G) in the majority of cases of severe anæmia and considerable increase occasionally (Cabot and Richardson 1919) Experimental anæmia in rats has resulted in slight cardiac hypertrophy at hæmoglobin levels of 10 G per cent and considerable hypertrophy (weight at least twice normal) at levels of 2 to 3 G per cent (Forman and Daniels 1930-1) According to Grunberg (1930) hypertrophy is invariable in man when the hæmoglobin is 15 per cent or less and does not occur at all when the hæmoglobin is 66 per cent or more

These findings harmonise with the behaviour of the cardiac output in relation to hæmoglobin levels and there can be little doubt that enlargement depends on increased work

*Clinical diagnosis* Knowledge of cardiovascular behaviour is of little value in making a diagnosis of anæmia and is of no value at all in determining the nature of the anæmia It is helpful however in differential diagnosis especially between anæmia the anxiety states and bacterial endocarditis Thus an anxiety state may present with the same group of symptoms including pallor and there may be cardiac over action and functional systolic murmurs The pallor however, is due to peripheral vasoconstriction and does not affect the conjunctivæ or the mucous membranes and it is less obvious in the palms of the hands the nail beds too are more likely to be cyanosed than pale In anæmia pallor is often waxy chalky or lemon tinted according to its severity and type The cardiovascular dynamics are quite different Over action of the heart and tachycardia in the anxiety states are associated with little or no rise in cardiac output there is peripheral vasoconstriction rather than vasodilatation and the diastolic blood pressure tends to be raised in casual readings the stroke volume tends to be reduced and the pulse may be small the circulation time and venous pressure are normal There are however exceptions to this general pattern about 10 per cent of patients with an anxiety state having a hyperkinetic circulation probably caused by an excess of circulating adrenaline

A type of case that may cause confusion is one that presents with pallor low grade fever petechiæ splenomegaly over action of the heart and a loud systolic murmur at apex or base Bacterial endocarditis may be sus

pected especially when there is a diastolic basal murmur as well and the pulse is collapsing yet all these features may be due to anæmia alone

*Treatment* All cardiovascular changes due to anæmia are reversible if the anæmia is treated successfully Cardiac remedies are rarely required apart from urgent measures in the event of acute pulmonary œdema The danger of ill judged or too rapid intravenous infusion has already been mentioned

## THE HEART IN PREGNANCY

### *PHYSIOLOGY*

There is now sufficient evidence to state with confidence that the hyper kinetic circulation of pregnancy begins to develop during the second month is well established by the end of the third month, increases slightly and gradually to the thirty second week and thereafter declines Much of this evidence has been summarised by Morgan Jones (1951)

Clinically the palms flush the extremities are hot the digital vessels throb capillary pulsation may be demonstrated the pulse is full and bounding the heart rate quickens the venous pressure rises the soft tissues become more tense and there may be slight œdema The heart itself is hyperdynamic the cardiac impulse is forcible and displaced slightly to the left aortic and pulmonary systolic murmurs heard at apex and base advertise the increased blood flow a loud third sound confirms rapid ventricular filling and X rays may reveal slight diastolic enlargement Ectopic beats are common The electrocardiogram often shows a prominent S wave in lead I and a conspicuous Q wave and inverted T wave in lead III (fig 21 04) due to rotation of the heart

Special tests reveal the following

(1) Oxygen consumption is increased by 15 to 20 per cent (Burwell 1937 1938)

(2) The cardiac output increases by 50 per cent (Palmer and Walker 1949 Hamilton 1949)

(3) Retention of sodium and water results in considerable hæmodilution the increase of plasma volume reaching a maximum of 45 per cent above normal by the thirty second week (Cohen and Thomson 1936 Thomson *et al* 1938) after which diuresis sets in (Chesley 1943)

(4) The general venous pressure rises as a result of the increased blood volume sometimes considerably the venous pressure in the legs is particularly high owing to the local obstructing effect of the enlarged uterus (Burwell *et al* 1938) Compression of the inferior vena cava is common in the supine position and the fall in right atrial pressure and cardiac output that may result from pooling of blood in the legs may cause faint ness and seriously interfere with physiological studies

The circulatory effects of pregnancy are attributed chiefly to the in

creased blood volume whilst the rise in oxygen consumption and a uterine arterio venous shunt (Burwell 1938) are contributory

Whilst the normal heart tolerates the added load easily enough diseased hearts may not When trouble occurs it usually *begins* early often by the end of the third month The *onset* of heart failure proper occurs with increasing frequency up to the end of the thirty second week after which it steadily declines (Hamilton and Thomson 1942)

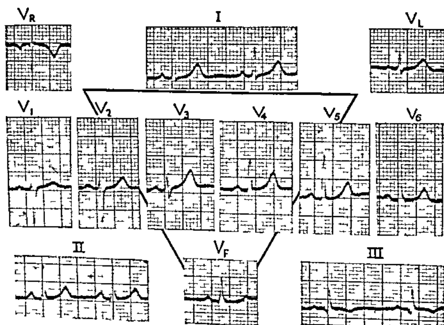



Fig 21 04—Electrocardiogram showing characteristic appearances associated with pregnancy

*Frequency and types of heart disease associated with pregnancy*

Heart disease was recognised in 1 3 per cent of 80 422 pregnant women analysed by Haig and Gilchrist (1949) Of their 1 100 heart cases 94 per cent were rheumatic 3 6 per cent congenital 1 8 per cent hypertensive and 0 6 per cent miscellaneous Similar figures (see table) have been published by Hamilton (1935) Morgan Jones (1951) and many others

Hypertension associated with toxæmia of pregnancy is obviously excluded from these statistics since this occurs in 5 per cent of all pregnancies Toxæmia is particularly dangerous in cases of heart disease not because of the hypertension (except in relatively rare cases of hypertensive heart disease) but because of the sodium and water retention

The mortality from heart disease in pregnancy averages 4 5 per cent (Jensen 1938 Jones 1951) but naturally varies greatly according to the

| NO OF PREGNANT WOMEN WITH HEART DISEASE | NATURE OF HEART DISEASE (frequency per cent) | | | | AUTHORS |
|---|---|---|---|---|---|
| | RHEUMATIC | CONGENITAL | HYPER TENSIVE | MISC | |
| 1 335 | 93 | 5 2 | — | 1 8 | Hamilton (1935) |
| 1 100 | 94 | 3 6 | 1 8 | 0 6 | Haig and Gilchrist (1949) |
| 485 | 90 | 6 8 | 1 | 1 1 | Morgan Jones (1951) |

severity of the lesion If patients are classified according to their grade of previous effort intolerance as defined on page 521 then the mortality from heart disease increases from about 0 4 per cent in grades 0 to 2A 5 3 per cent in grade 2B and 22 6 per cent in grades 3 and 4 (Jensen 1938) These figures were based on 1,428 cases collected from the literature over 90 per cent of them rheumatic Hamilton (1947) reported somewhat similar figures in a series of 1 335 cases of heart disease in pregnancy (93 per cent rheumatic) the mortality in grades 0 to 2A was 2 per cent as it was in non pregnant controls with heart disease of similar degree whereas in grades 2B to 4 the mortality was 18 per cent, compared with 6 7 per cent in non pregnant controls When there was atrial fibrillation the maternal mortality was 32 per cent (8 per cent in non pregnant controls)

Infant mortality should also be considered In Hamilton s series this was 8 6 per cent in the favourable group 31 per cent in the unfavourable group and 50 per cent when there was atrial fibrillation

Figure 21 05 which has been constructed from data published by Jensen (1938) shows that mortality increases steadily throughout pregnancy and reaches its climax during labour itself and the ensuing 24 hours

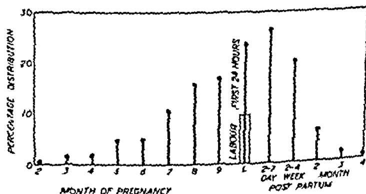



Fig 21 05—Chart showing when death occurs in fatal cases of heart disease associated with pregnancy

nearly 24 per cent of the 462 deaths analysed occurring at this time but the puerperium is also dangerous 26 per cent of the deaths occurring between the second and seventh day after delivery and 20 per cent during the next fortnight Werko (1954) regards the first 48 hours after delivery as the most dangerous period

The commonest causes of death are congestive heart failure (36 per cent) and pulmonary œdema (27 5 per cent) (Jensen 1938) The latter is chiefly responsible for death during pregnancy, the former for death during or after delivery (Morgan Jones 1951)

### *General Management*

Irrespective of the type of heart disease present the following general rules are widely accepted

1 Patients with grade 0 to 1 effort intolerance should not ordinarily be dissuaded from having a family and should experience little extra trouble during pregnancy and the puerperium

2 Patients with grade 2B to 4 effort intolerance who cannot be radically improved by present methods of treatment should be advised not to have a family and pregnancy should be terminated within the first three months if already present If the nature of the cardiac lesion is beyond foreseeable therapeutic developments sterilisation should also be carried out but not otherwise If the pregnancy is already advanced it is usually best to allow it to continue to its natural conclusion

3 Patients with grade 2A effort intolerance should be considered individually and social factors may be taken into account

4 If the cardiac lesion calls for surgical treatment the operation is best undertaken before pregnancy if the patient is already pregnant the operation should be carried out without delay if effort intolerance is grade 2B or more or deferred for a year or so if effort intolerance is grade 0 to 2A The pregnancy itself should not be terminated and sterilisation is unjustified

5 The best means of combating the adverse effect of pregnancy on the cardiovascular system is the low sodium diet supported if necessary by mercurial diuretics mictine diamox or resins Digitalis is not indicated when pulmonary œdema is due to mitral stenosis but is helpful in cases of atrial fibrillation and congestive heart failure Prolonged rest preferably in bed should be enforced until the situation is well in control

## *RHEUMATIC HEART DISEASE AND PREGNANCY*

There are some who maintain that any woman who has rheumatic heart disease should be advised against having any children They argue that pregnancy affects her adversely and that the strain of bringing up children shortens her life Others feel that to forfeit so much human happiness on these grounds is both undesirable and unnecessary Is life so precious to

prolong if so much of its meaning is taken away? Moreover available statistics barely support the first argument Thus in four combined series collected by Jensen (1938) the average age of death in spinsters or nulliparous women with mitral stenosis was 36 6 in married women with families it was 40 3 Again, Bunim and Rubricius (1948) could find no significant difference in the life histories of 169 rheumatic mothers and 215 rheumatic childless women Of course, the childless women may have been advised against pregnancy owing to the severity of their condition so that the two groups may not be strictly comparable there is insufficient evidence on this point It is certain however that many women with mitral stenosis unaware that there is anything wrong with them have large families and lead normal lives until the lesion is discovered in later life

Over 90 per cent of all cases of heart disease associated with pregnancy are rheumatic and at least four fifths of these have mitral valve disease usually stenosis The increased blood volume and raised cardiac output result in further elevation of the left atrial pressure and since the rapidity of the change leaves little time for the development of physiologically protective mechanisms hæmoptysis and acute pulmonary œdema are relatively common Less frequently and chiefly in those with a high pulmonary vascular resistance uncontrolled atrial fibrillation myocardial fibrosis or active rheumatic carditis the extra load results in congestive heart failure Pulmonary embolism increases the mortality during the puerperium

The majority of patients with uncomplicated mitral stenosis who experience serious trouble during pregnancy *begin* to develop *symptoms of* increasing pulmonary congestion towards the end of the third month conversely if all is well at the end of the first trimester without prophylactic treatment little trouble is likely to arise later Clinically when assessing the physiological situation due allowance must be made for the fact that 60 per cent of normal women experience breathlessness during pregnancy (Hamilton and Thomson 1942) and that a slight rise of venous pressure is normal

When considering the question of future pregnancy in cases of rheumatic heart disease it is vitally *important to make sure* whether surgical treatment is possible or not In cases of *aortic or mitral incompetence* for example pregnancy should be avoided or terminated within the first few months if effort intolerance is grade 2A or more for these lesions cannot yet be corrected surgically and any deterioration may well prove disastrous moreover both aortic and mitral incompetence must be advanced before grade 2 effort intolerance develops

*Cases of mitral stenosis* on the other hand are relatively safe if symptoms are already moderate or severe, valvotomy should be carried out before pregnancy if effort intolerance is only grade 1 to 2A and the pulmonary vascular resistance normal valvotomy should be deferred and pregnancy allowed to take its natural course if serious symptoms then develop

valvotomy may be performed during pregnancy which need not be terminated Cases of mitral stenosis with a raised pulmonary vascular resistance require valvotomy before pregnancy irrespective of the grade of effort intolerance for they are likely to develop congestive heart failure late in pregnancy or during the puerperium with or without pulmonary embolism When the patient is already pregnant valvotomy should be performed as soon as possible and if the operation is technically successful the pregnancy should be allowed to continue

Although *rheumatic aortic stenosis* may be relieved surgically the high mortality and relatively indifferent results of the present operation are not reassuring and patients with this lesion should be managed in respect of pregnancy like patients with aortic incompetence

Previous statistics showing no difference in the mortality rate from mitral stenosis and the other valve lesions in relation to pregnancy do not apply now that mitral stenosis can be relieved surgically

Normal pregnancy is safe after technically successful valvotomy in cases with previous mitral stenosis but toxæmia can be very dangerous when there is mild residual stenosis pulmonary œdema then occurring very readily One of the writer s post operative cases died under just these circumstances and necropsy revealed a partially split valve with an orifice measuring approximately 2 5 × 1 cm

Retention of sodium and water must be countered strenuously with a rigid low sodium regime

Cases of active rheumatic carditis are probably best terminated as soon as the state of the heart permits for there is no knowing what the sub sequent course will be and a relapse later in pregnancy may prove very serious

When pregnancy is not advised prevention is best insured by a simple sterilising operation Termination of pregnancy is by therapeutic abortion in the first three months by abdominal hysterotomy from the fourth to the sixth month by induced labour or by Cæsarean section during the seventh and eighth months by natural means or by Cæsarean section at term The choice must rest with the obstetrician

## CONGENITAL HEART DISEASE

Any form of congenital heart disease compatible with adult life may obviously be associated with pregnancy In practice the more common lesions include atrial septal defect patent ductus arteriosus pulmonary stenosis with normal aortic root coarctation of the aorta ventricular septal defect and Fallot s tetralogy—in that order of frequency With the exception of ventricular septal defect all these lesions can now be repaired or relieved surgically and if severe enough to warrant such treatment the operation should be carried out before pregnancy If the patient is already pregnant surgical treatment should not be delayed and the pregnancy need not then be terminated Patients who have had severe congenital heart -

disease cured repaired or sufficiently relieved surgically may have one or more babies subsequently without ill effect Mild congenital lesions are no bar to pregnancy and do not adversely influence obstetrical mortality

*Atrial septal defect* of mild or moderate degree is compatible with many normal pregnancies If severe however it should be repaired with the aid of hypothermia, preferably before, but if necessary during the early months of pregnancy

*Patent ductus arteriosus* is now treated surgically as a routine however mild If a small duct is discovered for the first time during pregnancy it is better to defer operative treatment but ducts of moderate or large size are better ligated without delay

*Severe pulmonary stenosis* has been relieved during pregnancy on several occasions and patients operated on previously have had normal pregnancies subsequently The second statement also applies to cases of Fallot's tetralogy who have been successfully relieved by pulmonary valvotomy or infundibular resection

*Coarctation of the aorta* may be discovered for the first time during pregnancy on account of the hypertension Although the majority of cases go through to term safely a few end disastrously with rupture of the aorta and to avoid this risk surgical repair is probably best undertaken at once if the condition is diagnosed within the first three months If not recognised until later however it may be better to defer the operation and to allow the pregnancy to proceed delivering the baby by means of Cæsarian section to avoid the risk of vascular accidents during labour (Benham 1949)

Since *ventricular septal defect* cannot yet be repaired satisfactorily severe cases should avoid pregnancy or should have the pregnancy terminated in the early months Cases of mild or moderate severity run no special risk Sterilisation is not justified because successful surgical repair may soon be possible

## BACTERIAL ENDOCARDITIS

Before the introduction of penicillin the life of the fœtus was the main consideration The situation is now reversed however and every effort should be made to save the mother As heart failure is now the chief cause of death from bacterial endocarditis, termination of pregnancy may often be desirable

## THYROTOXICOSIS

One of the few known factors that may aggravate or precipitate thyrotoxicosis is pregnancy It follows that thyrotoxic women should be advised against pregnancy until they are cured Improvement on rest and iodine or as a result of thiouracil treatment is not enough such cases tend to relapse during pregnancy At least a year should pass after partial thyroidectomy or thiouracil cure before conception should be considered

If a woman is thyrotoxic and already pregnant therapeutic abortion should be considered during the first three months if not seen until gestation is more advanced it may be wiser to take the patient to term with the aid of thiouracil Subtotal thyroidectomy is better deferred owing to the risk of relapse The dose of thiouracil must be the minimum that is effective for there is some danger of its causing goitre in the fœtus the simultaneous administration of small doses of iodine or thyroid may prevent this

*HYPERTENSION*

High blood pressure discovered during pregnancy may be due to chronic persistent hypertension (usually essential) or to toxæmia of pregnancy Essential hypertension may be aggravated by pregnancy but with rest diet and sedatives mild cases can be taken to term Nevertheless women with high basal blood pressures (above 160/100 mm Hg) should be advised against pregnancy in view of the increased risk of toxæmia the high infant mortality (66 per cent according to Browne 1947) and the chances of serious aggravation For similar reasons pregnancy should be terminated in women with relatively high pressures in the first three months Hypertension associated with toxæmia of pregnancy is a separate problem and will not be considered here

## ARTERIO VENOUS FISTULA

Arterio venous fistula may be congenital (circoid aneurysm) or acquired (usually as a result of a perforating wound) and may occur in any situation particularly in the brain limbs or lung

*Physiology*

Experimentally an artificial arterio venous fistula between the femoral artery and vein for example results in an immediate fall of blood pressure slight elevation of the venous pressure acceleration of the pulse and rise of cardiac output whilst locally the distal part of the leg becomes œdematous the skin cold and the toes occasionally gangrenous (Holman 1937) Physiologically the fistula acts as a zone of low resistance in the arterial circulation The drop in blood pressure is due to the fall in total peripheral resistance the greatly increased blood flow through the fistula tends to raise the venous pressure the tachycardia is due to the fall in blood pressure acting on carotid and aortic baroreceptors the rise in venous pressure usually being too slight to stimulate the Bainbridge reflex the increased cardiac output is due to a combination of the fall in total peripheral resistance which encourages the heart to empty itself more completely the slight rise of venous filling pressure and the tachycardia Locally œdema of the leg has been attributed to great elevation of the femoral venous pressure coldness pallor and gangrene to a diminished blood flow distal to the lesion for it is much easier for blood to pass through the fistula than through the normal channels (Holman 1937)

After a variable time several important changes take place The blood volume increases and raises the venous pressure more conspicuously the cardiac output is thus augmented and the blood pressure gradually restored The shunt through the fistula is increased by these changes but sooner or later a state of balance is reached Locally, the vessels carrying the shunt become dilated even aneurysmal the artery below the fistula is affected as well as that above, because blood entering the distal part of the terminal artery from collateral channels is forced backwards by the peripheral resistance to the fistulous zone of lower resistance The dilated arteries that accommodate the increased flow become thin walled and the veins receiving the flow at a higher pressure than that to which they are accustomed become arterialised in other words both become anatomically adjusted to the new pressure With the increased blood volume and total cardiac output the blood flow to the distal part of the leg is not only restored but often becomes greater than normal The leg becomes hot and the veins distended and when initial œdema has subsided the leg usually remains larger than its fellow (Holman 1937)

The physiology of congenital and acquired arteriovenous fistula is the same as that found experimentally both in the initial and later stages of development Local effects were well described by Reid (1925) amongst others and Cohen *et al* (1948) confirmed that the blood flow in the affected limb distal to the fistula was diminished in early cases and increased in cases of long duration The increased blood volume was demonstrated by Rowntree and Brown (1929) and the raised cardiac output by Warren *et al* (1947) and Cohen *et al* (1948) In congenital cases the increased vascularity of ununited epiphyses in the affected limb may lead to considerable hypertrophy of one arm or leg (Horton 1932)

## *CONGENITAL CIRCOID ANEURYSM*

Circoid aneurysm consists of a twisted mass of dilated vessels in which artery and vein are in direct communication One or more superficial hæmangiomas may be seen elsewhere or there may be a family history of such nævi

*The cerebral type* may give rise to epilepsy subarachnoid hæmorrhage or ophthalmoplegic migraine Examination may reveal a systolic murmur heard best through the eye ball on the affected side or sometimes over the skull The diagnosis may be proved by finding an unduly high oxygen saturation in samples of blood obtained from the ipsilateral jugular vein The lesion may be localised by means of angiography 10 to 20 ml of 70 per cent diodone or other radio opaque substance being injected rapidly into the carotid artery and skiagrams of the cerebral vessels being obtained at the appropriate moment The condition should be distinguished from berry aneurysm and from Sturge s disease in which facial and pial nævi without arterio venous communications are associated with calcification of brain substance epilepsy mental retardation and glaucoma (Nussey and



Fig 21 06 (a)—Skiagram showing a congenital arterio venous aneurysm of the lung The appearances bear some resemblance to those of pulmonary tuberculosis
(b) Angiocardiogram showing diodone filling the aneurysm

*A k oul dgment t Dr Cl l B k*

Miller 1939) Treatment consists of ligation of the common carotid artery on the side of the lesion if after trial compression hemiplegia or other serious ischæmic symptoms do not occur The risk of such an untoward event increases progressively with the age of the patient

*Circoid aneurysm in a limb* presents similar features to those of its traumatic cousin It may be situated anywhere from the shoulder or pelvic girdle to the hand or foot There is usually an increase in blood flow to the limb which may be longer and larger than its fellow Occasionally however there is ischæmic atrophy in one or more digits distal to an aneurysm in the hand or foot The veins stand out are sometimes varicose and may exhibit arterial pulsation and the skin temperature is raised It may be possible to locate the aneurysm with precision by observing the effect on the local and general circulation of compressing the various arteries of the limb at appropriate points An impressive machinery murmur and thrill may be appreciated over the fistula itself Venous blood from the affected limb may be more saturated with oxygen than venous blood from the unaffected limb The exact location and construction of the aneurysm may be demonstrated by means of angiography Treatment is more difficult than in traumatic cases Excision is usually impossible owing to the diffuse nature of the lesion moreover affected vessels are physiologically abnormal and fail to constrict when injured so that severe and

prolonged hæmorrhage may follow surgical interference Ligation of the main vessels leading to the aneurysm (above and below) may be possible but deep X-ray therapy is usually best

*Congenital arterio venous aneurysm in the lung*, which is associated with telangiectasis elsewhere in 50 per cent of cases (Baer *et al* 1950), causes venous blood from the pulmonary artery to be shunted directly into the pulmonary veins and thence into the arterial circulation, at the same time the blood flow through the rest of the lung may be reduced the steep pressure gradient through the aneurysm offering the easier pathway The result is a lowered arterial oxygen saturation in the region of 70 to 75 per cent (Burchell and Clagett 1947) central cyanosis polycythæmia and clubbing Most of the cases reported have been in children or young adults Hæmoptysis has occurred in 50 per cent The heart itself is normal but there may be a continuous machinery murmur over the affected part of the lung A skiagram may show a rounded or irregular opacity (fig 21 06a) which on fluoroscopy may be seen to pulsate tomograms may reveal a dilated artery and vein in close relationship to the abnormal shadow and angiocardiograms may show the abnormal vessels filled with diodone (fig 21 06b) (Baker and Trounce 1949) Lesions may be single or multiple unilateral or bilateral Calcification may occur in the wall of an aneurysm (fig 21 07) One case (a girl aged 9) seen by the author died with cerebral abscess The condition should be distinguished from patent ductus arteriosus helping to correct pulmonary or tricuspid atresia Treatment by lobectomy or pneumonectomy is curative unless there are several widely distributed aneurysms (Barnes *et al* 1948)



Fig 21 07—Calcification in the wall of an arterio-venous aneurysm
*Acknowledgment t D Ch l B k*

*Congenital coronary arteriovenous fistula* is very rare but is mentioned in view of its peculiar interest to cardiologists Details of a few cases that have been reported including a new one of my own are given in the accompanying table It will be noticed that four were symptom free and were detected only because of the continuous thrill and murmur When this was maximum in the third left space the fistula was between the left circumflex coronary artery and the coronary sinus when it was maximum low down

| AUTHOR | AGE | SEX | SYMPTOMS | SITE OF A V MURMUR OR THRILL | E C G | X RAY | CORONARY ARTERY INVOLVED | DIAGNOSIS |
|---|---|---|---|---|---|---|---|---|
| Halpert (1930) | 54 | M | Nil | — | — | — | Right | P M |
| Paul *et al* (1949) 3 | 9 | M | Nil | Right sternal edge 4th and 5th space | Normal | Normal | Right | Clinical and operative |
| Cross (quoted by Paul *et al*) | 16 | M | Nil | 3rd and 4th left spaces | — | — | ? left circumflex | Operation |
| Davison *et al* (1955) | 58 | F | Congestive heart failure | 2nd 3rd 4th left spaces | A fib QRS balanced | General enlargement congested lungs | Left circumflex | P M |
| Wood | 60 | M | Nil | 4th and 5th spaces right sternal edge | Normal | Calcified A V aneurysm | Right | Clinical X ray |

the right sternal edge the fistula was between the right coronary artery and the coronary sinus Cardiac catheterisation was carried out in only one instance and a left to right shunt at atrial level was demonstrated the pulmonary blood flow was 6 9 litres per minute the systemic 3 1 (Davison *et al* 1955) The diagnosis could have been made had samples from the coronary sinus been obtained In my own case the diagnosis was obvious clinically and radiologically (fig 21 08) and catheterisation was not justified Of these five cases this was the only one with calcification



(a) Right anterior oblique view



(b) Left anterior oblique view

Fig 21 08—Calcified arterio venous fistula between the right coronary artery and coronary sinus

## *ACQUIRED ARTERIO VENOUS ANEURYSM*

The great majority of acquired arterio venous aneurysms are due to perforating gunshot wounds in war and are seen most often in connexion with the femoral brachial or carotid arteries Occasionally they may be syphilitic mycotic or artificial Arterio venous shunting may also occur in highly vascular structures such as the thyroid gland in severe thyrotoxicosis or as a result of overdosage with thiouracil (page 879) the uterus in pregnancy (page 903) and the bones in active Paget s disease (page 917)

The local signs and the effect on the general circulation are similar to those in experimental arteriovenous fistula At first the affected limb swells the skin becomes cold and there is danger of peripheral gangrene When a state of balance is reached and compensatory adjustments have been made the œdema subsides and the limb becomes warmer than its fellow The

veins distend and may pulsate A coarse machinery murmur and thrill are invariable over the lesion it elf

The general circulation is hyperkinetic and if the shunt is large enough paroxysmal ca diac dyspnœa or signs of congestive heart failure may develop as observed by Reid (1920) If the shunt is temporarily obliterated by digital compression of the femoral artery just above the lesion, the pulse rate falls 10 to 30 beats per minute (Branham s sign) the blood pressure rises 10 to 15 mm Hg the venous pressure falls slightly and the cardiac output falls (Stead and Warren, 1945) but capillary pulsation is accentuated (Lewis and Drury 1923) Slowing of the pulse is due to the rise in blood pressure and is abolished by atropine (Kramer and Kahn 1946)

Cardiac enlargement is almost certainly due to the raised cardiac output and increased stroke volume The hyperkinetic circulation is maintained by tachycardia and raised venous filling pressure whilst the peripheral resistance is further reduced by vasodilatation in skin and muscle

*Treatment* Any arterio venous aneurysm large enough to influence the general circulation should be repaired Smaller lesions may be left alone if causing no local symptoms and some of them become obliterated spon taneously Every effort should be made to repair the artery by lateral suture or graft so that the normal circulation is preserved (Junghann 1943) Ligation of artery and vein above and below the aneurysm is less satis factory the re ulting circulation through the brain or limb being sometimes inadequate Simple ligation of the artery above the fistula was condemned as long ago as 1886 by Bramman for this frequently results in peripheral gangrene

## THE HEART AND CIRCULATION IN BERI BERI

In modern civilised communities pure beri beri is rare the clinical picture being commonly influenced by deficiencies in vitamins other than aneurin ($B_1$) and by associated conditions especially chronic alcoholism Aneurin (thiamine) in association with other components of the vitamin B complex is found chiefly in unpolished rice marmite liver yeast wheat and other grains It is used by the body in carbohydrate metabolism its ch ef known function being concerned with the oxidation of pyruvic acid which is formed from lactate When there is insufficient aneurin carbo hydrate metabolism is held up at this point and an excess of pyruvic acid accumulates in the blood (Peters 1939) It follows that any condition in which carbohydrate metabolism is excessive predisposes to beri beri in that aneurin requirements are heavier When in addition the vitamin B intake is reduced at the same time as in chronic alcoholism vomiting of pregnancy and thyrotoxic crises beri beri may well develop

The normal requirement of aneurin is about 1 mg daily for an adult and is supplied adequately by the ordinary European diet Special ulcer diets however unless supplemented may be deficient and psychoneurotic

patients with severe anorexia and vomiting may not receive a sufficient supply of the vitamin Beri beri was common in German concentration camps and Japanese prison camps during the second world war, although usually complicated by other vitamin deficiencies, and has always been relatively common in the Far East when the basic food has been polished rice

Aneurin deficiency is rarely gross in civilised communities and so the presence of some additional factor is commonly needed before the effects of slight deficiencies are brought to light Under these conditions beri beri is atypical for such patients are apt to be middle aged or elderly and the classical signs may be masked by hypertension coronary sclerosis or emphysema in these mixed cases no clear picture of beri beri develops (Konstam and Sinclair 1940)

*Behaviour of the heart and circulation* The pure disease was studied in Java by Wenckebach (1928 1934) The essential features included a hyper kinetic circulation vasodilatation enlargement of the heart and dilatation of the pulmonary artery Few accurate cardiac output studies have been carried out but the clinical description and the swift circulation time (Weiss and Wilkins 1936–37) leave little doubt that it is high Heart failure may develop suddenly and fulminating cases occur in which death results within 24 to 48 hours of alleged onset of symptoms (Hashimoto 1937) Even in Great Britain cases have been described in which heart failure has occurred remarkably suddenly and unexpectedly leading to a rapidly fatal issue (Wood 1939)

The cause of the hyperkinetic circulation is vasodilatation The drop in peripheral resistance encourages the heart to empty itself more completely whilst the fall in blood pressure causes reflex tachycardia As in all hyper kinetic circulatory states associated with a lowered peripheral vascular resistance (except chronic anæmia) retention of sodium and water by the kidneys increases the blood volume raises the venous pressure and so further increases the cardiac output The remarkable quietening of the circulation that follows the injection of 1 ml of pitressin and the stormy reaction to 1 mg of subcutaneous adrenaline (Wenckebach 1928) confirm the important role of vasodilatation The sudden rise in pulse rate and cardiac output that follow the subcutaneous injection of 10 mg of mecholin or the inhalation of amyl nitrite demonstrate clearly the effect of vaso dilatation on the circulatory hæmodynamics in normal subjects

The heart itself shows little specific at necropsy, the disturbance being biochemical not structural

*Diagnosis* The clinical diagnosis of cardiovascular beri beri rests on an appropriate dietetic history the demonstration of a hyperkinetic circula tion radiological appearances showing conspicuous dilatation of the pul monary artery associated with overaction and general enlargement of the heart the response to pitressin and adrenaline associated polyneuritis and on the finding of a raised blood pyruvic acid or reduced amounts of

aneurin in blood (Jansen 1938 Sinclair 1938) or urine (Harris *et al* 1938 McAlpine and Hills 1941)

Peripheral neuritis usually begins with pain in the calves on walking similar in character to intermittent claudication Associated weakness of the legs marked tenderness of the calves numbness and tingling of the fingers and toes loss of deep tendon jerks and glove and stocking anæsthesia are usually found

Evidence of deficiencies in other vitamins especially of the vitamin B group is helpful in proving inadequacy of the diet

*Treatment* It must be stressed that the symptoms of beri beri may begin abruptly and that the course of the disease may be fulminating death occurring within a few days of the onset Once the diagnosis has been made there may be no time to lose Again the possibility of vitamin $B_1$ deficiency should always be borne in mind in any case of heart failure of obscure origin Here is one of the fatal forms of heart disease which is curable

The patient should be put to bed immediately and aneurine hydro chloride should be given at once intravenously in an initial dose of 50 to 100 mg The effect is dramatic if not given too late Subsequent doses should be of the order of 10 to 20 mg per day for a fortnight orally or parenterally and followed by an adequate diet An abundance of the other components of the vitamin B group is also advised

Fulminating cases should benefit by repeated injections of pitressin (1 ml 4 hourly) until the vitamin has had time to work but care must be taken to avoid hydræmia by keeping the salt and water intake as low as possible

Chronic alcoholics cases of severe thyrotoxicosis Simmond s disease or anorexic nervosa and women vomiting in pregnancy should be given 2 to 5 mg of aneurin daily as a precautionary measure

## PAGET S DISEASE OF BONE

The hyperkinetic circulation associated with extensive active Paget s disease was first clearly demonstrated by Edholm Howarth and McMichael in 1945 The general cardiovascular findings closely simulate those associated with arterio venous aneurysm In the case described by Edholm *et al* the blood flow through actively diseased bones was estimated to be 3 to 4 litres per minute and the total cardiac output was 13 litres per minute The venous pressure was elevated and there was dependent œdema Further observations on other cases of active Paget s disease have shown that the heart is not usually overloaded for it is capable of increasing its output by means of tachycardia or a greater rise of venous filling pressure on the other hand paroxysmal cardiac dyspnœa may then occur (Mc Michael 1947)

Paget s disease also encourages metastatic calcification especially Monckeberg s sclerosis and calcification of the valve rings of the heart

Extension to the interventricular septum may involve the bundle of His or its branches with the production of complete heart block or bundle *branch block respectively (Harrison and Lennox, 1948)*

Cor pulmonale secondary to thoracic deformity from Paget s disease has also been described (Wilks 1869)

*Diagnosis* If aortic incompetence and valve calcification are both present the clinical diagnosis of Paget s disease may be overlooked in favour of atherosclerotic aortic valve disease As long as the condition is borne in mind however diagnosis is easy for skiagrams of the bones show characteristic changes and the blood alkaline phosphatase is very high

## HEPATIC FAILURE

It has become increasingly evident that advanced disease of the liver may lead to a hyperkinetic circulatory state in addition to the well known palmar flush and cutaneous spider nævi The usual cause is secondary carcinoma but common cirrhosis and even serious infective hepatitis may be responsible It appears that the liver normally detoxicates some vaso depressor substance and that this substance accumulates when the organ is failing (Shorr *et al* 1945) vasodilatation results in the same chain of physiological adjustments that have been described in arteriovenous fistula and beri beri The remarkable effect of hepatic failure on the circulation may be seen sometimes in advanced cases of heart failure when vaso dilatation replaces peripheral vasoconstriction

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CHAPTER XXII

# TRAUMATIC LESIONS OF THE HEART AND GREAT VESSELS

## SPONTANEOUS LESIONS

SPONTANEOUS traumatic lesions of the heart or great vessels include dissecting aneurysm of the aorta, rupture of a hypoplasic aorta or syphilitic aortic aneurysm, ruptured valve cusps in bacterial endocarditis, rupture of a congenital, syphilitic or mycotic aneurysm of a sinus of Valsalva into the right side of the heart, rupture of chordæ tendineæ in rheumatic or bacterial endocarditis, and rupture or perforation of the heart or ventricular septum secondary to cardiac infarction or ventricular aneurysm. The majority of such lesions have been described elsewhere as complications of the diseases mentioned. Only dissecting aneurysm and rupture of an aneurysm of a sinus of Valsalva into the right side of the heart remain to be considered here.

### *DISSECTING ANEURYSM*

#### *Definition*

Dissecting aneurysm was so called by Lænnec (1826) and means dissection of the media of the aorta by extravasated blood that has penetrated between its coats from the vasa vasorum or from the lumen of the vessel.

#### *Incidence*

About 1 per cent of all sudden deaths are due to dissecting aneurysm (Mote and Carr, 1942). Hospital records, which include relatively few such deaths, give an approximate incidence of one dissecting aneurysm in every 450 necropsies. The Registrar General's figures for 1953 show it to be responsible for about 0.5 per cent of all cardiac deaths in England and Wales. Men are more susceptible than women in the ratio of 2.5 : 1 (Levinson *et al.*, 1950). Patients are commonly between 50 and 60 years old, but 24 per cent are under 40 (Schnikter and Bayer, 1944), and cases have been recorded in children (e.g. Galbraith, Gardner and Hardwick, 1939). About 50 per cent of dissecting aneurysms in women have occurred during pregnancy (Schnikter and Bayer, 1944).

#### *Etiology and pathology*

Virchow's original conception that dissection follows an intimal tear at the site of an atheromatous ulcer is no longer tenable, for a tear at such a site is now known to be rare (Shennan, 1934). Although hypertension and atheroma are usually associated, they are not essential; the intima may be normal and not even ruptured (Tyson, 1931).

Dissection is always within the media commonly begins in the ascending aorta and appears to be closely related to cystic medial necrosis (Erdheim 1929) The cause of such necrosis is unknown Tyson s thesis that it was due to obliterative endarteritis of the vasa vasorum has not been con firmed Cystic necrosis without dissection may be found sometimes in routine necropsies (Moritz, 1932 Rottino 1939) Whether hæmorrhage into the diseased media commonly follows an intimal tear, or whether it comes from the vasa vasorum (the intimal tear then being due to secon dary rupture) remains uncertain When the intima is intact hæmorrhage obviously cannot come from the lumen of the aorta On the other hand intimal tears may undoubtedly be primary for they may occur in healthy ascending aortas without subsequent dissection (Peery 1942) Occasionally hæmorrhage occurs into an area of cystic necrosis of the media without dissection the hæmatoma then becoming organised and causing no trouble (Shennan 1934)

It has recently been suggested that cystic medial necrosis and dissecting aneurysm may be due to defective formation or excessive destruction of chondroitin sulphate the chief mucopolysaccharide of the ground sub stance of the aorta (Ponseti and Baird 1952) These authors noted the high frequency of dissecting aneurysm and kyphoscoliosis in growing rats fed on 50 per cent sweet pea meal the toxic agent being $\beta$ aminopropionitrile The fault in the ground substance that results from this agent is believed to be responsible for both skeletal and aortic flaws Bean and Ponseti (1955) found that seven out of 27 clinical cases of dissecting aneurysm had gross kyphoscoliosis

Dissection not infrequently complicates congenital hypoplasia of the aorta usually part of Marfan s syndrome an inherited mesodermal dyscrasia which may well incorporate faulty ground substance A similar flaw may explain the frequency of aortic rupture or dissection in cases of coarctation of the aorta

Dissection may spread proximally and involve the root of the aorta causing aortic incompetence occasionally the coronary arteries are dis sected and occluded Dissection usually spreads distally however may travel the whole length of the aorta and may proceed along any of its branches Ischæmic effects from occluded visceral or parietal vessels are common The majority of cases die from external rupture usually into the pericardium (Strassmann 1947) sometimes into the left pleural cavity or elsewhere Occasionally dissection associated with an intimal tear in the ascending aorta ruptures back into the lumen of the vessel at some distal point forming an alternative or double aortic channel (double barrelled aorta) This is found in the majority of cases that recover (Shennan 1934)

*Clinical features*

Dissection of the aorta may be precipitated by effort (Gager 1928) but is more often spontaneous A typical attack begins suddenly with severe

pain in the centre of the chest or in the præcordial area The pain may be gripping tearing shooting, or vice like and usually lasts for hours it may radiate to the head and neck to the back—less often to the arms Later in the attack it may spread to the lumbar regions or abdomen and occasionally to the legs depending on the extent of the dissection In perhaps half the cases however pain is slight or absent (Baer and Goldburgh 1948)

Breathlessness is nearly as common as pain (Hamburger and Ferris 1938) and syncope occurs in about 10 per cent of cases (Levinson *et al* 1950) Attacks may therefore closely resemble coronary thrombosis but in cases that survive the blood pressure usually remains high and the electrocardiogram normal moreover, dilatation of the aorta may often be seen in skiagrams (fig 22 01) (Wood, Pendergrass and Ostrum 1932) Fever and leucocytosis are the rule not the exception (Baer and Goldburgh 1948)

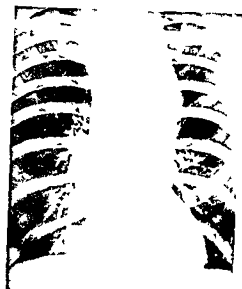


Fig 22 01 —Dissecting aneurysm of the aorta

Other findings depend upon the site and extent of the dissection upon which branches of the aorta are occluded and upon the site of external rupture Aortic incompetence may develop when the root of the aorta is dissected (Weiss 1935) and is being noted with increasing frequency (David *et al* 1947) myocardial infarction may occur if the left or right coronary artery is occluded giving rise to the appropriate electrocardiographic pattern (Wainwright 1944) Pericardial friction is heard occasionally and hæmopericardium may be recognised before death

Dissection of major arteries leads either to occlusion of the vessel or to increased amplitude of pulsation due to spontaneous periarterial sympathectomy (Weisman and Adams 1944) Occlusion of one or other or both carotid arteries may cause hemiplegia mental confusion or coma of the anterior spinal artery, paraplegia of arteries to the limbs loss of the peripheral pulse and perhaps ischæmic pain of the renal artery, hæmaturia —and so on Occasionally a pulse that has been absent may re appear as a result of rupture re entry (Lawrence 1935) A systolic murmur and thrill may develop over partly occluded vessels including the aorta (McGeachy and Paullin 1937) Left hæmothorax is found in about 12 per cent of cases (Baer and Goldburgh 1948) Hæmorrhage into the mediastinum may be responsible for cough and dysphagia An abdominal mass may become

palpable Hæmoptysis hæmatemesis and hæmaturia occur occasionally

Cases that survive the original dissection may present themselves later with congestive heart failure associated with aortic incompetence When there has been no history of pain such cases have usually been diagnosed erroneously as syphilitic aortic incompetence despite negative Wassermann reactions (Gouley and Anderson 1940 Flaxman 1942)

*Angiocardiography* may help to prove the diagnosis (Golden and Weens 1949) but is not advised in the acute or subacute stage

*Prognosis*

According to Shennan (1934) about 10 per cent of all cases of dissecting aneurysm recover from the attack usually owing to rupture re entry The majority succumb later to heart failure either as a result of aortic incompetence or from associated hypertensive heart disease

*Treatment*

No treatment is likely to influence the course of dissection Morphine should be given freely to combat pain If the patient survives the initial attack he should be kept in bed for at least a month

## *RUPTURE OF AN ANEURYSM OF AN AORTIC SINUS (SINUS OF VALSALVA) INTO THE RIGHT ATRIUM RIGHT VENTRICLE OR PULMONARY ARTERY*

Aneurysm of one of the aortic sinuses may be congenital syphilitic or mycotic Rupture of such an aneurysm into the pericardium or left pleural cavity is immediately fatal but perforation into the right atrium ventricle or pulmonary artery leads to a well defined clinical syndrome which may be compatible with many years of active life

*Incidence*

The condition is rare indeed the author has only encountered and investigated four living instances Congenital cases may occur in young adults syphilitic cases in later life and mycotic at any age About 80 per cent of reported cases have been in men aged 20 to 67 (Oram and East 1955)

*Physiology*

Rupture into the right atrium causes a large arteriovenous shunt into that chamber overloading of the right heart and the rapid development of congestive failure Cardiac catheterisation reveals a left to right shunt at atrial level Perforation into the right ventricle may similarly overload the right heart blood samples and intracardiac pressures are similar to those in ventricular septal defect (R A P 0 R V P 12 P A P 15 mm Hg S V C and R A samples 44 to 45 R V and P A samples 28 ml oxygen unsat per litre in a case seen by the author)



(a) Anterior view showing engorged pulmonary circulation enlargement of the left ventricle and resection of the 5th rib on the left side (the case having been operated on for patent ductus)



(b) Second oblique view showing enlargement of the left ventricle and dilatation of the pulmonary artery

Fig 20 02—Case of ruptured mycotic aneurysm of aortic sinus into the pulmonary artery

Perforation into the pulmonary artery sets up similar features to patent ductus arteriosus (fig 20 02) In one such case investigated by the author due to a perforated mycotic aneurysm from bacterial endocarditis (cured by penicillin) samples from the right atrium and ventricle showed 67 to 70 ml oxygen unsaturation per litre whereas pulmonary artery samples were only 33 to 36 ml unsaturated The mean right ventricular pressure was 31 mm of Hg above the sternal angle and the pulmonary artery pressure 63 mm Hg

*Clinical features*

Pain may occur from involvement of the orifice of one or other coronary arteries but is otherwise absent The onset is usually signalled by the rapid development of congestive heart failure but not necessarily The two cases mentioned above were by no means incapacitated and one is still alive 15 years after the onset

The chief signs are a loud machinery murmur accompanied by a thrill over the base of the heart but at a lower level than that associated with patent ductus arteriosus accompanied by signs of aortic incompetence and by features resembling those of ventricular septal defect or patent ductus according to the site of the perforation

*Prognosis*

Rapid deterioration to a fatal outcome is said to be the rule (Abbott 1919) but this may be because the diagnosis is usually only made at autopsy Three of the author s four cases are not only alive but relatively well the fourth died of heart failure

## EFFECTS OF DIRECT INJURY

Direct injury to the heart may be caused by stab or gunshot wounds and very rarely by diagnostic procedures such as needling the pericardium The literature on the subject has been well surveyed by King (1941) and by Barber (1944)

### *GUNSHOT WOUNDS*

A bullet or piece of shrapnel may perforate the heart through and through may lodge in the myocardium or pericardium with or without perforation of one or more chambers or may graze the surface of the heart without causing death In an analysis of 25 instances of war wounds involving the heart made in conjunction with Nicholson in 1945 the relative incidence of such lesions was as follows

| | |
|---|---|
| Near misses | 4 |
| Grazes or tangential wounds | 4 |
| Through and through perforation | 3 |
| Foreign body in pericardium | 7 |
| Foreign body in myocardium | 7 |

Of 1 640 consecutive penetrating chest wounds the heart was directly or indirectly injured in 1 7 per cent The immediate result is hæmopericardium and the rapid development of cardiac tamponade If a foreign body passes close to the heart or lodges within half an inch of its surface a transient pericardial serous effusion may develop If the patient does not die from cardiac tamponade or hæmorrhage into the pleural cavity complete recovery may follow whether or not a metallic foreign body remains in the heart

The chief complication during convalescence is recurrent acute pericarditis this is nearly always associated with the presence of a foreign body either in the pericardium or closely connected with it (Wood 1945) it rarely arises when a bullet is embedded deeply in the myocardium The attacks tend to be severe with pain fever tachycardia gross electrocardiographic changes and the rapid development of a sterile serous effusion which may cause cardiac tamponade They usually last about a week The first attack may occur at any time during convalescence up to about three months after the injury and may recur several times at intervals of about a month Of five such cases studied by the author in the second world war all finally recovered three without interference and two after removal of the foreign body by Nicholson (1945)

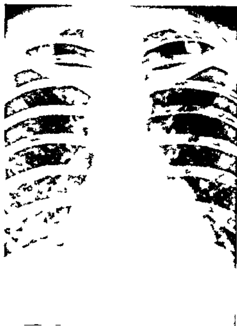


Fig 22 03—Machine gun bullet imbedded in the right atrium



Fig 22 04—Skiagram taken in 1937 showing machine gun bullet embedded in the heart since 1917

A second complication is coronary thrombosis during convalescence when a pericardial foreign body is in contact with a major coronary vessel but this was observed only once

*Diagnosis* The possibility of cardiac injury should be considered in all cases of gunshot wounds of the trunk or neck especially if the missile is judged to have been directed towards the heart or if its direction is not known for certain Early diagnosis depends upon recognising the signs of cardiac tamponade or hæmopericardium (page 661) An electrocardiogram may be most helpful by showing the presence or absence of the pericardial T pattern

Intracardiac or pericardial foreign body may be readily detected by means of fluoroscopy its movement with the heart beat aiding recognition but it may be easily overlooked in skiagrams

*Treatment* It is impossible to say how many lives might be saved by early surgical repair of cardiac wounds In the second world war the majority of cases that survived long enough to be evacuated to general hospitals recovered

Relief of cardiac tamponade by paracentesis may be life saving both in the early stages or during a later attack of acute pericarditis Metallic foreign bodies lodged in the pericardium are best removed in view of the danger of recurrent pericarditis Although none of the attacks witnessed proved

fatal the episodes were most alarming Intracardiac foreign bodies should probably be removed if superficial and left alone if deep

*Prognosis* Only one of the twenty five patients mentioned previously died but as already stated these were favourable cases in that they had survived until evacuated to a general hospital

Follow up studies are incomplete but the worst case with three attacks of recurrent pericarditis and a machine gun bullet embedded in the wall of the right atrium was alive and well two years after being wounded (fig 22 03)

In 1937 the author had the opportunity of investigating a healthy man with a machine gun bullet embedded in his heart since 1917 An unsuccessful attempt to remove the bullet was made at the time An electro cardiogram taken by Sir James MacKenzie showed the usual pericardial T pattern Twenty years later effort tolerance was excellent there were no abnormal physical signs and the electrocardiogram was normal X rays showed the bullet still embedded in the heart in close relationship to the apex of the interventricular septum (fig 22 04) This case was reported in detail by Grey Turner (1941) On the whole it seems likely that the ultimate fate of these patients is favourable

## *STAB WOUNDS OF THE HEART*

Direct injury to the heart in civil life is usually due to single or multiple stab wounds the majority of which penetrate the right ventricle The clinical physiological radiological and electrocardiographic features of cases that have survived long enough to receive medical aid have been chiefly those of hæmopericardium (Wood 1937) Death from hæmorrhage into the pleural cavity or from cardiac tamponade may be prevented by timely surgical repair

Even when patients appear to be holding their own it is probably wise to evacuate the blood clot and to repair and sterilise the wound as soon as possible for hæmorrhage may continue or recur and serious cardiac tamponade develops in most cases Moreover if tamponade is unrelieved too long acute coronary insufficiency may seriously impair the function of the myocardium and when it is finally relieved death may result from acute heart failure The development of a bulge on the left border of the heart simulating the appearances of ventricular aneurysm should not deter the surgeon for this is likely to prove no more than a localised pericardial hæmatoma (fig 22 05)



Fig 20 05—Localised pericardial hæmatoma superficially resembling a cardiac aneurysm

## EFFECTS OF INDIRECT INJURY

Indirect injury to the heart may be caused by crushes blows falls or blast The effects include sudden death from ventricular fibrillation or standstill rupture of the aorta rupture of one or more chambers of the heart rupture of the aortic or mitral valve, hæmopericardium myocardial bruising auricular fibrillation and heart block Coronary occlusion and subsequent angina pectoris or cardiac infarction may also occur but their relationship to trauma is less well understood

### *SUDDEN DEATH*

A heavy blow to the region covering the heart may cause sudden death from ventricular fibrillation or cardiac rupture both naturally and experimentally in dogs (Bright and Beck 1935)

There have been numerous instances of sudden death resulting from relatively minor trauma of a kind quite incapable of damaging the heart The catastrophe is then ascribed to ventricular fibrillation or cardiac standstill induced by neurogenic shock Sudden immersion in icy water extreme fright or a blow over the heart insufficient to cause material damage may each act in this way This type of death is similar to that which may be caused by a small pulmonary embolism in experiments in dogs the size of the embolism being quite insufficient to embarrass the circulation and death being preventable by atropine The mechanism is probably a vagal reflex

Rupture of the aorta is more likely to occur from a fall, especially if there is congenital hypoplasia as in many cases of coarctation Hæmorrhage is usually into the pleural cavity or pericardium

### *RUPTURE OF THE HEART*

Rupture of one or more chambers of the heart following trauma is not always immediate nor does it always cause sudden death A myocardial bruise may result in cardiac aneurysm or delayed rupture usually during the second week as described by Bright and Beck These authors collected over 150 cases of traumatic rupture of the heart from the literature and found the incidence of the various chambers involved to be as follows

| | |
|---|---|
| Left ventricle | 37 |
| Right ventricle | 31 |
| Left auricle | 30 |
| Right auricle | 36 |
| More than one chamber | 13 |
| Interventricular septum | 11 |
| Interauricular septum | 1 |

It will be appreciated that this distribution is very different from that seen with spontaneous rupture secondary to cardiac infarction when the left ventricle is nearly always responsible

The latent interval was studied by Warburg (1938) It occurred in 15 out of 51 cases proved at necropsy A small tear may behave similarly to a direct penetrating wound that causes delayed death from hæmopericardium usually within a few days A bruise may rupture at any time within six weeks (Barber 1938) or occasionally after a longer interval Cardiac aneurysm resulting from a bruise may rupture years afterwards (Joachim and Mays 1927)

During the quiescent phase the patient may seem relatively well any discomfort being attributed to the bruise on the chest and he may continue his normal activities including sport (Priest 1939) In other cases symptoms may result from hæmopericardium or from any of the other effects to be described presently

*Diagnosis*

If the patient is seen alive after cardiac rupture the signs and symptoms are those of hæmorrhage into the pericardium or pleural cavity The combination of collapse rapid thready pulse and a high jugular venous pressure from cardiac tamponade is very suggestive if discovered within a month of injury There may be no evidence of external damage to the chest wall and the history of the accident may not be mentioned for it may not appear to be connected with the illness If the possibility of previous trauma is considered the diagnosis is usually obvious

*Treatment*

Immediate surgical repair is the only hope of saving life

## *HÆMOPERICARDIUM*

Symptoms and signs of pericarditis with or without hæmopericardium are relatively common after indirect cardiac trauma particularly perhaps after blast injury They provide useful evidence of cardiac damage but do not necessarily indicate its nature Surgical interference is only warranted if there is tamponade which usually signifies cardiac rupture or serious coronary hæmorrhage Many cases have recovered spontaneously (Smith and McKeown 1939)

## *MYOCARDIAL BRUISING*

Crushing of the chest direct blows over the heart and blast may all cause myocardial contusion the clinical picture resembling that of myocardial infarction including the characteristic electrocardiographic changes or heart failure without pain (Barber 1940 Barber and Osborn 1941)

Following a direct blow in the præcordial region, electrocardiographic changes may occur which are indistinguishable from those of posterior myocardial infarction (Anderson 1940) In these cases it may be assumed that the right coronary artery has been injured anteriorly

The chief danger of myocardial contusion is delayed rupture as previously described

Treatment consists of rest in bed for six weeks semi starvation a low sodium intake mersalyl if necessary sedatives, and avoidance of digitalis

## RUPTURED AORTIC CUSP

Indirect trauma sometimes ruptures an aortic cusp There may or may not be underlying aortic valve disease congenital or acquired The lesion results in the abrupt development of aortic incompetence which throws a heavy burden upon an unprepared left ventricle so that failure of that chamber is likely to ensue

The diagnosis is suggested by the sudden onset of orthopnœa paroxysmal cardiac dyspnœa or pulmonary œdema following a serious fall or other violent accident and is confirmed by the discovery of a loud, harsh sometimes musical aortic diastolic murmur often accompanied by a thrill especially if the valve was known to have been normal previously

The prognosis may be good if the patient survives the immediate insult but death from heart failure within six weeks is a grave risk (Barber 1938 1944) Treatment consists of six weeks rest in bed in order to allow time for adequate compensation and may have to be directed towards combating left ventricular failure It must be understood that a degree of aortic incompetence which would be well tolerated and consistent with years of active life if it had developed slowly may cause death from acute heart failure when it occurs abruptly just as acute hypertension may cause left ventricular failure and pulmonary œdema whereas much higher pressures may be tolerated when developing slowly in benign hypertension

## TRAUMATIC MITRAL INCOMPETENCE

A severe fall or sudden blow over the heart or other violent accident may occasionally rupture chordæ tendineæ or tear one of the mitral cusp particularly if already diseased The lesion is rare but there are many well authenticated instances (Barber and Osborn, 1937) A clinical diagnosis may be made from the history if it is known that no murmur was present before the accident if a loud harsh mitral systolic murmur is heard when the heart is first examined after the accident if there is no evidence of previous rheumatic valve disease and if confirmatory signs of organic mitral incompetence develop (page 506)

A number of cases have died from congestive heart failure within a few hours or weeks of the accident and others have developed mitral stenosis later (Barber, 1938) On the other hand the accidental discovery of symptomless mitral incompetence attributable to trauma need cause little alarm such cases behaving like rheumatic mitral incompetence with a healthy myocardium

## HEART BLOCK

There have been a number of instances of asphyxia in which hæmorrhage has taken place around the bundle of His with resulting heart block Several

cases have been seen at necropsy by the author, and a good example was observed during the 1940–1 London air raids

A woman of about 35 known to have been in previous good health was rescued in a partly asphyxiated condition from beneath a lot of debris Examination shortly afterwards revealed not only complete heart block but also gross signs of hemi Parkinsonism presumably due to hæmorrhage into the bundle of His and into the substantia nigra She declared that she had received no severe blow on her chest nor significant crush but had been partly asphyxiated by dust for about one hour

Heart block may also result from a blow over the heart or from a fall on the chest (Coffen, 1930 Warburg 1938), and has been so produced experimentally in dogs (Kissane, 1937) Hæmorrhage into the conducting system is presumably responsible The lesion may be transient or permanent the prognosis depending on the presence or absence of Stokes Adams fits and upon the rate of the idioventricular pace maker, but on the whole it is fairly good provided there is no more serious injury and provided the heart muscle is sound

## *AURICULAR FIBRILLATION (OR FLUTTER)*

Several cases of auricular fibrillation caused or precipitated by blows have been reported (Kahn and Kahn 1928) particularly in the elderly (Barber 1938) Bramwell (1934) records a case in which auricular fibrillation was probably initiated by a head injury, and Hay and Jones (1927) describe one due to electric shock

The mechanism whereby head injury may cause auricular fibrillation is particularly interesting though still obscure There is reason to believe that parasympathetic activity may be culpable Thus digitalis which stimulates the vagus, may cause auricular fibrillation and there is a form of sinus bradycardia due to vagal influence which is associated with paroxysms of flutter or fibrillation In experiments on certain animals fibrillation may be induced by vagal stimulation Not only head injury but also meningitis Meniere s syndrome and probably other intracranial disturbances may excite this rhythm change

## *CARDIAC INFARCTION AND ANGINA PECTORIS*

As already described myocardial contusion may give rise to clinical and electrocardiographic features similar to those of myocardial infarction and may also result in cardiac rupture or aneurysm There appears to be a closer relationship however between trauma and ischæmic effects For example an anterior injury to the chest may cause a posterior left ventricular lesion clinically indistinguishable from a cardiac infarct and classical angina pectoris may develop for the first time immediately after trauma (Campbell 1939) Moreover the subsequent course of these cases may be that of ordinary ischæmic heart disease It is possible that blows crush injuries and blast may injure the anterior coronary vessels either by causing sub

intimal hæmorrhage in an atherosclerotic artery or more directly and thus cause acute coronary occlusion or secondary thrombosis After such an event subsequent angina pectoris would be readily understood Great care must be taken in diagnosing traumatic angina however, for many persistent chest pains following injury represent compensation neurosis

Treatment consists of three to six weeks rest in bed followed by one to three months convalescence to allow time for the development of adequate collateral vascularisation The prognosis depends upon the degree of underlying coronary disease as well as upon the amount of damage inflicted On the whole it is not dissimilar to that in ischæmic heart disease in general

## MEDICO LEGAL ASPECTS

Employees are entitled to compensation if it can be shown that trauma has initiated or aggravated a cardiovascular disability Even a case of syphilitic aneurysm that ruptures during the course of work receives compensation Patients with established heart disease may deteriorate after an accident and this aggravation is equally compensated The benefit of doubt is always given to the patient and in a court of Law or a tribunal it is difficult to convince a judge or president that trauma has not adversely affected the cardiovascular system Yet a firm stand must be taken over the development of cardiac neurosis Left inframammary pain is especially liable to become persistent and intractable if linked to the idea of compensation and the physician must be prepared to make a categorical statement to the effect that this is not organic and is not due to the accident that it origin lies in the mind and in the emotions and its growth runs parallel with the conscious or subconscious desire for gain

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CHAPTER XXIII

# CARDIOVASCULAR DISTURBANCES ASSOCIATED WITH PSYCHIATRIC STATES

THE cardiovascular system may be profoundly influenced by psychological or psychiatric states through the medium of the autonomic nervous system The stimulus is emotional and appears to act on the central vegetative nuclei in the region of the hypothalamus We are all familiar with the uncomfortable thudding of our hearts during moments of fear and most of us have witnessed a fainting attack provoked by the sight of something that is at once queer and frightening The physiological basis for such phenomena is relatively simple sympathetic or adrenergic activity may cause palpitations by accelerating the pulse elevating the blood pressure and strengthening the heart beat parasympathetic or cholinergic activity may induce syncope by retarding the pulse lowering the blood pressure and weakening the heart beat

Cardiovascular upsets of this kind sufficient to bring the patient to seek medical advice almost invariably indicate psychiatric disorder for the effects of emotion within the limits of common physiological experience are too transient and too familiar to disturb a normal individual Moreover in psychiatric states such symptoms may be persistent or may be provoked too readily The syndrome so produced has been called soldier s heart irritable heart disordered action of the heart (D A H ) cardiac neurosis effort syndrome autonomic imbalance neurocirculatory asthenia etc Such terms should be discarded in favour of the correct psychiatric diagnosis but the words effort intolerance may be added with advantage preferably in brackets when clinically important Historically one may speak of Da Costa s syndrome to cover all previous nomenclature (Wood 1941)

The syndrome is characterised by a group of symptoms which unduly limit the subject s capacity for effort or which upset his peace of mind at rest by a number of signs which depend upon disturbance of the autonomic nervous system and by an underlying psychiatric disorder The cardinal symptoms are breathlessness (93 per cent) palpitations (89 per cent) fatigue (88 per cent) left inframammary pain (78 per cent) and dizziness (78 per cent) or syncope (35 per cent) The cardinal signs are those of functional disturbance of the respiratory vasomotor sudomotor and muscular systems The psychiatric disorder is commonly an anxiety state but may be almost anything with high emotional content including the psychoses

It should be understood that there is no essential difference between effort syndrome and cardiac neurosis they are merely clothed differ

ently the former in battle dress the latter in nylon In civil life the condition accounts for 10 to 15 per cent of all cases referred to cardio vascular clinics it is common in children and occurs more often in women than in men the ratio being 3 2 It has a preference for the emotional races especially the Jews and the Italians In the first world war there were some 60 000 'effort syndrome casualties n the British forces in the second a more enlightened view was taken, the majority of these cases receiving appropriate psychiatric labels and management

## CLINICAL FEATURES

The cardinal symptoms and signs have already been mentioned, they will now be discussed in more detail

*Breathlessness* These patients experience a true sensation of breathlessness in circumstances that would not affect a normal person It is not only a question of breathlessness on effort but patients will say they are unable to obtain a satisfying breath, or that they feel a sense of suffocation and this is confirmed objectively by frequent deep sighs Sometimes they complain of attacks of noctural dyspnœa which may be confused with bronchial asthma or with paroxysmal cardiac dyspnœa careful questioning however should reveal their psychosomatic nature especially by probing the precipitating anxiety dream and by unmasking the associated panic state Further evidence of functional respiratory disorder may be obtained by noting hurried irregular and shallow breathing A simple and illuminating test is forced hyperventilation The patient is asked to breathe deeply and rapidly for one minute A normal individual experiences dizziness and sometimes slight tingling of the fingers and toes When told to stop he passes into a state of apnœa lasting about 20 seconds The psychoneurotic especially the hysteric dramatises his subjective sensations and when told to desist usually continues forced breathing explaining later that he felt breathless Since dizziness is due to cerebral vasoconstriction induced by carbon dioxide washout it is clear that such psychoneurotics experience breathlessness when the carbon dioxide content of the arterial blood is so low as to cause apnœa in controls The respiratory stimulus must therefore come from higher centres The maximum breath holding time is another useful test Normal subjects have no difficulty in holding the breath for at least 30 seconds but patients with Da Costa s syndrome usually give up very quickly 30 per cent of them in less than 10 seconds moreover in contrast to controls they show little distress when they reach the breaking point

*Palpitations* Cardiac overaction resulting from emotional stimulation plays an important role in the induction of cardiac neurosis It is a common psychiatric event for some intangible fear to become linked to something more easily understood and remote from the real difficulty For example a psychoneurotic with a morbid fear of heights may develop palpitations

when ordered to climb a ladder If the idea that palpitations may denote some disorder of the heart occurs to him he at once embraces the possibility and proceeds to advance the theory in all seriousness for it disguises his true fear which might be thought shameful and protects him from the danger Although a successful defence mechanism in these two respects the manœuvre is baneful because it provokes a new fear that of heart disease and sudden death this new fear aggravates the palpitations and so closes a vicious circle

The palpitations of anxiety states are associated with sinus tachycardia elevation of the blood pressure increase in cardiac output and probably with strengthening of the heart beat These features are due essentially to emotional stimulation of a normal adrenergic system

*Fatigue* Patients often complain that they do not feel refreshed when they wake in the morning that their sleep has been of no benefit to them They also feel tired and listless during the day, and are unduly fatigued by effort The symptom is usually attributed to anxiety dreams and to emotional conflicts

*Left inframammary pain* Psychosomatic pain is usually situated in the left inframammary region but may be higher lower more central or more lateral it may radiate down the left arm It is commonly described as aching or as sharp and stabbing in quality but occasionally it is constricting or cramp like Although pain may occur during effort it is more frequent afterwards it is also common at night and may prevent the patient sleeping on the left side sometimes it is capricious and bears no relationship to any known factor Sharp twinges are momentary and acute stitch like pain may last several minutes but the classical ache usually continues for hours It thus usually differs from angina pectoris in its eccentric site its quality relationship to effort and duration i e in every important respect Occasionally however as may be inferred from the description given above psychosomatic pain may be situated near the left border of the sternum referred to the left arm constricting in quality and measured in minutes In such cases it may well be misinterpreted There is usually some odd remark however or something in the patient s manner which should warn the physician and encourage him to launch a critical cross examination The precise history of angina pectoris will not be shaken by this but that of an anxiety state alters and becomes more complicated and confused when elaborated

Left inframammary pain is important because it seems to convince the patient that his heart is diseased and it is not unnatural that he should think thus of a pain arising so close to it In the psychoneurotic this creates a morbid fear of death and catastrophe and so closes another vicious circle

The exact mechanism of the pain is obscure It is immediately abolished by the intramuscular injection of 2 ml of novocaine at the site of maximum intensity or tenderness Cutaneous or subcutaneous anæsthesia has no

effect This indicates that it is not referred but arises locally in muscle or fascia and suggests that it is related to fibrositis' and low back pain It may be initiated by fatigue or strain of respiratory muscles in cases with respiratory neurosis by strain of certain muscular attachments involved in such actions as cranking an engine or lifting a heavy weight, by incessant minimum trauma from the light hammer blows of an overacting heart or by faulty posture It is exaggerated and perpetuated by the belief that it arises in the heart

*Dizziness* Dizziness means momentary faintness, transient unsteadiness light headedness , or a far away feeling It does not refer to spinning as in vertigo It may occur on sudden movement of the head on standing up abruptly or during effort It is readily reproduced by hyperventilation when it is attributed to cerebral vasoconstriction Orthostatic dizziness is related to orthostatic hypotension, and is due to inadequate circulatory adjustments on assuming the erect posture It is probable that other forms of dizziness are also due to diminished cerebral blood flow induced by autonomic disturbance Transient loss of consciousness due to temporary failure of the cerebral circulation occurs at one time or another in 20 to 30 per cent of these cases

*Sweating* Sweating is a helpful diagnostic feature because in the majority of instances it is confined to the axillæ the palms of the hands and the soles of the feet These are emotional sweat areas Thermal sweating and that induced by cholinergic drugs, have a different distribution being much more widespread Sweating associated with effort may begin emotionally but is soon thermal Thyrotoxic sweating is also thermal The hands are the best single guide if sweating is confined to the palms the stimulus is emotional if the backs of the hands are also involved other causes should be considered Undue sweating is mentioned or admitted by 80 per cent of these cases and is seen objectively in about two thirds

*Headache* Headache is a common complaint (72 per cent) and is either vague or throbbing In assessing the reality of the physical basis of the throbbing type it is helpful to ask the patient to count the throb aloud or better to tap out the rhythm digitally while the observer checks this against *the pulse rate in true vascular headache they must* coincide in hysteria they do not Unilateral carotid compression is also useful for it abolishes vascular headache on the same side but it either aggravates or has no effect upon hysterical pain Throbbing vascular headache may be induced by the intravenous injection of 1 mg of histamine or by trinitrin or amyl nitrite in some cases It is closely associated with exaggerated pulsation of the cerebral arteries (Pickering 1939) It is seen clinically not only in the anxiety states but also in fevers and in acute alcoholism It occurs spontaneously in migraine Improvement depends upon better autonomic regulation, which in turn depends upon successful treatment of the underlying anxiety state



Fig 23 01—Clas ical facies build and posture of a case of Da Costa s syndrome Painted by Ian Tillard (l fe size portrait in the museum of the Post Graduate Medical School of London)

## PHYSICAL SIGNS

Signs of autonomic disturbance serve to check the validity of psychosomatic symptoms Most have already been mentioned but they will be recapitulated and grouped here for convenience

General

- Tense dejected or diffident manner
- Dull weak or listless facies
- Soft quiet timid voice

Cardiovascular

- Tachycardia (30 per cent)
- Overaction of the heart (44 per cent)
- Blood pressure in the region of 150/90 mm Hg (27 per cent above)
- Deceleration time over 2 minutes in effort tolerance test (33 per cent)
- Acrocyanosis (44 per cent)
- Flushes (36 per cent)

Respiratory

- Frequent deep sighs (32 per cent)
- Rapid irregular or shallow breathing occasionally hyperventilation (21 per cent)
- Inability to hold the breath for 30 seconds (76 per cent)
- Dyspnœa instead of apnœa after forced breathing

Sudomotor

- Visible sweat on the palms of the hands (67 per cent)
- Sweat trickling from the axillæ (35 per cent)

Skeletal and Muscular

- Tremor of fingers usually coarse irregular and inconstant ( 6 per cent)
- Shakiness of voice and limbs
- Asthenic posture or poor physical development (41 per cent)
- Tenderness in area of left inframammary pain

A life sized portrait of one of these patients (fig 23 01) hangs in the library of the Postgraduate Medical School of London and surpasses any description The effort tolerance test consists of stepping on and off a chair ten times and counting the pulse rate before immediately after and subsequently at minute intervals until the resting speed is regained The deceleration time is abnormal (over 2 minutes) in 33 per cent of these patients

Physical signs of autonomic disturbance are helpful in distinguishing the malingerer and in assessing the severity of the case About 90 per cent of normal young adults do not show more than one of these signs and 50 per cent show none

## PSYCHIATRIC ASPECTS

Although the syndrome described may occur in any psychiatric state with high emotional tone it is usually associated with an anxiety state In many there are hysterical features and a large number show reactive depression

The family history is tainted with psychoneurosis in 50 to 60 per cent compared with 5 to 10 per cent in controls with or without organic heart disease About 66 per cent describe neurotic traits in childhood morbid fears especially of the dark of heights of water or of animals are frequent bed wetting stammering tics nightmares sleep walking and undue delicacy of health are common They are timid children far too dependent upon maternal protection At school kindly doctors and soft mothers protect them from the hazards of football swimming and the gymnasium

It is probable that predisposition to psychoneurosis is mainly hereditary but early environmental factors such as domestic strife insecurity suppression and maternal coddling play their part

There are many factors which may operate to bring about the adult syndrome and in any particular case one should never be satisfied with the discovery of only one or two It is fruitful to search for evidence of predisposition for a state of mind recently prepared for the development of psychoneurosis by external or by endogenous factors for precipitating agents for the growth of vicious circles and for motives for gain that aggravate and perpetuate the syndrome Proper assessment management and prognosis are impossible if any vital link is overlooked

Hereditary and environmental predisposition have already been discussed The mind is especially prepared for the development of psychoneurosis when in a state of confusion and unreality Head injuries may bring this about certain acute fevers are often responsible especially rheumatic fever influenza meningitis and diphtheria long hours of work in unpleasant and unhappy surroundings may be to blame

Precipitating factors are often multiple It is as if one or two could be coped with but when several occur one on top of the other mental equilibrium disintegrates They are usually closely linked with fear in some form or another The most obvious example is active service hence the high incidence of the disorder in war Fear of football and fear of swimming are common in childhood and may precipitate anxiety at school The fear of being unsuccessful of not being able to shoulder responsibility is a common cause of breakdown in civil life Insecurity or fear of the future is also common The adoption of a line of action contrary to established social custom may cause an anxiety state due to fear of discovery and public criticism Difficult personal relationships especially between husband and wife are often responsible Sex difficulties are important, but should not be over emphasised Financial worry unemployment fear of disease play their part To a timid sensitive character the

being found out of being thought a coward, of being proved inadequate of seeming a fool—and so of losing cast, is a very real and powerful emotional stimulus

The development of vicious circular patterns is interesting In this particular syndrome most vicious circles have a common basis and revolve round the *fear* of heart disease and sudden death The combination of breathlessness dizziness or syncope fatigue and especially palpitations and left inframammary pain provides convincing evidence of heart disease to the lay mind *All* these symptoms which are psychosomatic *in* mechanism may be produced by simple anxiety and may disappear rapidly as soon as the anxiety is resolved *But if* the patient takes the fatal step and believes that *they* are due to heart disease a vicious circle is at once established for a new and greater *fear* develops that of sudden death at any moment This constant anxiety operating consciously or subconsciously every second of the day and night increases the severity of the psychosomatic symptoms Under these circumstances the syndrome is maintained long after resolution of the original anxiety Superimposed upon this pattern or independent of it there develop various and often complicated conditioned *reflexes* until finally distressing autonomic reactions are so ingrained and so divorced from conscious thought as to be practically ineradicable Correct medical interpretation of early psychosomatic symptoms is of the utmost importance in the prevention of these pernicious grooves The doctor who misinterprets a boy s fear of water and accepts the pallor and palpitations as *signs* of heart disease who mistakes left inframammary pain *for* angina pectoris who *finding* an innocent systolic murmur diagnoses valvular heart disease who regards syncope *or* dizziness as a sign of cardiac weakness is *guilty* not only of *stupidity* and ignorance but is also *responsible* for turning *his* patient into a chronic and incurable psychoneurotic Even so *it* may be comforting to know that medical blunders of this kind will influence only 10 per cent of apparently normal individuals the great majority adversely affected showing evidence of predisposition

Finally there is the motive for gain This is seen in compensation neurosis and in war it is obvious at every medical board The inadequate personality of so many of these patients capitalises the symptoms What timid man indifferent to higher ideals will face the dangers of battle when the very symptoms of his fear offer him protection?

## DIFFERENTIAL DIAGNOSIS

The characteristic symptoms and signs associated with psychiatric disorder usually make the diagnosis easy The physical features have been stressed because the psychiatric state may not be obvious until the mind has been deeply probed This is well shown by comparing the conclusions drawn at the special investigation centres for effort syndrome during the

first two world wars at Hampstead in world war I where little attention was paid to psychiatry not more than 10 per cent were considered psycho neurotic at Mill Hill in world war II a psychiatric basis was proved in 94 per cent The diagnosis should be positive not dependent upon a process of exclusion it may stand even when organic disease is also found especially mild rheumatic heart disease benign hypertension and chronic bronchitis

Thyrotoxicosis may present difficulty to the inexperienced The common mistake is to diagnose an anxiety state as thyrotoxicosis rarely the reverse The difference is fully considered on page 874 and 878 Particular attention should be paid to the attitude and behaviour of the patient to the expression of the eyes to the colour and temperature of the hands to the distribution of sweating to the diastolic blood pressure and to the appetite

In children active rheumatic carditis may cause confusion vague muscle pains being mistaken for joint pains and tics for chorea

Attacks of violent palpitations in anxiety states are sometimes confused with paroxysmal tachycardia Accurate history taking and observation of an induced attack should prevent error The special points of difference are given on page 237

The distinction between left inframammary pain and angina pectoris has already been considered but real difficulty may arise In both the diagnosis depends largely upon the history and cannot be proved or disproved by the demonstration of psychoneurosis on the one hand or of organic heart disease on the other The matter is further complicated by the adverse effect of anxiety upon ischæmic heart disease for it may be so important a factor that its satisfactory resolution may temporarily relieve angina pectoris Occasionally the diagnosis remains doubtful until determined by the future course

The physician should be on his guard against pulmonary tuberculosis chronic undulant fever juvenile spondylitis spontaneous hypoglycæmia and certain endocrine disorders—especially the menopause Anæmia should be more obvious When the symptoms first arise during convalescence simple reassurance should be given and the final diagnosis deferred until it is clear that rapid recovery has or has not taken place

## TREATMENT

Treatment is never easy and is the more difficult the longer it is delayed Failure is certain if any essential factor in the development of the syndrome is overlooked so that a great deal of time must be spent on these patients Simple reassurance and some superficial explanation are quite inadequate

First the patient must feel that at last he has met a doctor who thoroughly understands his case secondly a complete physical examination supp by fluoroscopy and an electrocardiogram is necessary so that

respect unconditional reassurance Adequate explanation must follow, and will vary according to the chief symptoms The object is to convince the *patient that the symptoms are emotionally produced* One may *point out* how sudden fear causes palpitations sweating alteration of breathing and sometimes a fainting attack He will agree with this but may object that he feels no such fear One should then explain that great fear acting for a few seconds may be more than equalled by a tiny remote fear acting over weeks months or years a state called anxiety This step is difficult but the point must be carried Correct interpretation of anxiety dreams is of value *in demonstrating the power of subconscious emotion* Enlightenment and conviction may come suddenly if psychosomatic disturbance on some particular occasion or under certain specific circumstances can be explained *in the light of emotional experience*

For example a *patient at Mill Hill gave a history of a morbid fear of fireworks* in his boyhood conditioned by London air raids in his infancy Otherwise he was fit and strong He was called up in September 1939 was sent to France and *remained well until told one day to unload an ammunition lorry* On handling the shells he became curiously panic stricken developed gross psychosomatic symptoms and mis interpreted them thinking they meant heart disease A vicious circle was initiated he reported sick and finally arrived at a base hospital with an established effort syndrome When the link between his fear of handling fireworks and his handling shells for the first time was *pointed out* he was suddenly convinced of the truth of the explanation given for his symptoms and made a rapid and complete recovery But his fear of fireworks shells and *all other explosives* was unabated Treatment had only been *directed* towards the removal of effort intolerance by abolishing the misinterpretation and vicious circle that initiated and maintained it

As a rule however it is not enough to reassure and give an adequate explanation for by the time the patient consults a *physician the* syndrome is usually highly complex and conditioned reflexes are well ingrained To cut across such reflexes and vicious circles, one may encourage the patient to come to better terms with his symptoms He *fears them* because he thinks they are injurious and may result in sudden death He must be told they are harmless that they can never be more than a nuisance that he is already familiar with the worst they can do Once he *appreciates* the fact that if he no longer fears his symptoms he will cease to aggravate them the point is scored

If there is an hysterical motive for gain it must be *mentioned* and then ruthlessly *underlined* It is *remarkable* what little insight these patients have, and disconcerting how little shame

The methods so far outlined do not touch the underlying psychoneurosis and the *real treatment* has yet to begin The patient may be referred to a psychiatrist or if the causative factors seem clear the physician may prefer to deal with them himself There are always three things *to consider* the difficulties in *which the patient is floundering* his reaction, which is based

on his character and intelligence and his attitude towards his reaction The difficulties should be taken first sorted out and resolved as far as possible The help of social welfare workers may be enlisted in this respect The patient s reaction should be analysed and some psychiatric skill and knowledge are required to do this It is often possible to show that his reaction is based on false values ideas or beliefs Or one may simply explain just why he so reacts in order to give him insight It is impossible to outline precisely just what is required for every case is different and needs individual treatment If the problem has no satisfactory solution and if the patient s reaction cannot be altered favourably then at least he may learn to get on better terms with both Difficulties must be faced and not hidden away in the dark recesses of the mind highly personal matters should be fully discussed in a matter of fact way until they cease to seem so dreadful if a man is standing on a false pedestal he must learn humility and honesty and tread upon the good earth

Finally the background must be assessed With strong hereditary taints and bad early environment the outlook is poor and the aim should be to fit the patient into circumstances which will cause the least embarrassment This is a confession of failure At the other extreme if the stock is good and if there is no evidence of predisposition and if this is confirmed by the severity of the stress of anxiety causing the breakdown every effort should be made to cure the patient In other words one should deal with the environment when the prognosis is bad and with the patient when it is good

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(A full bibliography is contained in these three articles )

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